Tampere University

Ippa Seppälä

MODELLING NEURONAL POPULATIONS USING A MEAN-FIELD APPROACH

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ABSTRACT

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The human brain consists of roughly a hundred billion interconnected neurons that work together to give rise to higher-level brain functions like memory consolidation and emotions. Single-cell models for neurons have existed since the start of the 20th century, often taking the form of differential equation systems. Connecting these cell models to form a network leads to large coupled systems that can be very challenging - if not impossible - to solve analytically.

The mean-field approach borrowed from theoretical physics allows us to represent large networks of neurons by studying the mean behaviour of the population. This means that we can assume the behaviour of each and every cell to tend to a mean average in a network that is large enough, due to the asynchronous behaviour such biological networks tend to exhibit. The mean- field method simplifies a large network of spiking neurons down to a single distribution function that describes the time evolution of the probability density of the population when it moves across its state space. This leads to the Fokker-Planck equation representation of the neuronal system.

In this Master of Science Thesis we study the mathematics behind these mean-field methods and how they can be applied to different neuronal models. As the Fokker-Planck equation is a seminal part of the mean-field approach, we explain how it is derived using Markovian chains and the concept of Brownian motion. We then concentrate on three different models in closer detail and show the reader how to derive and solve the resulting differential equation systems. Lastly we discuss how these models differ from each other both mathematically as well as biologically, and compare their respective properties.

Keywords: neuron, neuronal, modelling, mean-field, mathematics, mathematical modelling

TIIVISTELMÄ

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Ihmisaivoissa on keskimäärin noin sata miljardia hermosolua, jotka kiinnittyvät toisiinsa muodostaen laajan viestintäverkoston. Näiden solujen yhteistoiminta mahdollistaa kaikki tuntemamme aivotoiminnot, kuten muistin toiminnan, aivojen laskentatehon ja tunteiden käsittelyn. Yksittäisiä hermosoluja on pystytty mallintamaan matemaattisesti jo 1900-luvun alusta asti differentiaaliyhtälösysteemien avulla. Aivojen mallintaminen populaationtasolla on kuitenkin laskennallisesti paljon haastavampaa, sillä yksittäissolumallien yhdisteleminen verkostoiksi johtaa yleensä systeemeihin, joiden ratkaiseminen analyyttisesti voi olla erittäin haastavaa, jos ei jopa mahdotonta.

Hermosolupopulaatioiden toiminnan kuvaaminen on kuitenkin mahdollista myös niinsanottujen keskiarvoistettujen kenttämallien, eli mean-field –mallien avulla. Tätä lähestymistapaa on alun perin käytetty teoreettisessa fysiikassa ja sen soveltaminen on luontevaa myös neurotieteessä. Mean-field -mallissa jokaisen hermosolun oletetaan käyttäytyvän koko verkoston keskiarvon mukaisesti. Tämä mahdollistaa kokonaisen solupopulaation toiminnan esittämisen yhden todennäköisyysjakauman avulla, jolloin solujen tilojen todennäköisyysmassan liike pystytään kartoittamaan ajan funktiona. Tässä yhteydessä hermosolujen tiloilla tarkoitetaan niiden aktiivisuutta, ja käyttäytymisen muutosta. Mean-field -lähestymistapa johtaa usein Fokker-Plank -yhtälöön, johon tässä tutkielmassa tullaan lähemmin tutustumaan.

Tässä Pro gradu -tutkielmassa tarkastelemme näiden keskiarvoistettujen kenttämallien matemaattisia ominaisuuksia, ja kuinka niitä voidaan soveltaa erilaisiin laskennallisen ja teoreettisen neurotieteen kysymyksiin. Me johdamme Fokker-Plack -yhtälön käyttäen Markovin ketjujen sekä Brownin liikkeen käsitteitä. Esittelemme kolme erilaista mean-field -mallia ja näemme, miten niiden taustalla olevat differentiaaliyhtälösysteemit voidaan ratkaista. Lopuksi vertailemme mallien biologisia ja matemaattisia ominaisuuksia, ja näemme miten ne eroavat toisistaan.

Avainsanat: neuroni, hermosolu, mallinnus, mean-field, matematiikka, matemaattinen mallinnus

Preface

The writing of this master thesis was supervised by Docent Marja-Leena Linne from the Faculty of Medicine and Health Technology and Asst. Prof. Lassi Paunonen from the Faculty of Information Technology and Communication Sciences at Tampere University. This research has received partial funding from the European Union's Horizon 2020 Framework Programme for Research and Innovation under the Specific Grant Agreement No. 785907 (Human Brain Project SGA2). The work was also supported by Academy of Finland (decision No. 297893). A special thanks to Mikko Lehtimäki for his continuous support.

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Ippa Seppälä

Contents

1 Introduction

The earliest computational models of the brain were developed in the first half of the 20th century. Since then scientists have been trying to understand the behaviour of the brain with the help of mathematical representations of neural cells. These cells are often best described by systems of differential equations that can be compared to and verified with the help of experimental data. This is fitting as we usually want to represent such phenomena with respect to time. In this thesis, we take a closer look at some single neuron models often used in computational neuroscience and familiarise ourselves with their properties, as well as derive a representation for a network of neurons. When these networks grow very large they exhibit specific behaviours not found in smaller populations. In modelling, this phenomenon can be mimicked by taking the network to the *mean-field* limit where the size of the population is assumed to be close to infinite. These so-called *mean-field models* are the principal point of interest of this thesis.

The main goal of this thesis is to examine the mathematical principles on which the mean-field approach is based. We introduce three different mean-field models that have very specific mathematical and biological differences. Here we will look at a *Fokker-Planck ensemble density model* [13], a *geometry based mean-field model*[27] and a *McKean-Vlasov type model with a dendritic compartment* [28]. We will see how the models in question are derived and how they differ from each other. It is important to note that whilst describing the same phenomenon on different levels of abstraction, all three of the models studied here have their place in theoretical neuroscience. Exploring the mathematical properties of each model will give us an idea of how neuronal activity can be approximated and how different functional properties of neurons can be accounted for by using varied mathematical approaches. Probability theory will be one of our main focuses as in all three models the behaviour of a large network of neurons is described by a stochastic process.

To understand the contents of this thesis, we will first introduce the neuron as a biological unit as well as its basic properties and functions. We will see how these properties translate to a mathematical representation and how these representations can be modified to acquire different types of neuronal models.

In Chapter 2 we briefly discuss the biological basis on which mathematical models of brain cells are built, and then give a quick overview of different types of models frequently used in theoretical neuroscience. We will give the reader an overview of the mean-field approach, its origins, and how the method can be applied to single cell models to derive a network representation.

In Chapter 3 we list some preliminary theorems and definitions that are necessary for following this thesis. Proofs of the theorems in this section are omitted, as they are not crucial for this topic. The reader is expected to have an un-

derstanding of the theory of ordinary differential equations (ODEs) as well as basic probability theory.

In Section 3.3 we introduce the reader to the topic of stochastic processes and how the random movement of particles ties into Einstein's *Brownian motion*. We see how it functions in both the single and the multivariate cases. We will also look at some helpful assumptions that can be made of the network when it tends to the mean-field limit.

In Chapter 4, we see how studying Markovian processes leads to the master equation, and how the equation itself is derived. We then use this expression to derive the Fokker-Planck equation and see how it can be used to find mean-field models for neural populations.

Then, in Chapter 4, we familiarise ourselves with the master equation, an integral part of this thesis. The master equation gives us the evolution of the probability of a system to occupy each discrete set of states with respect to continuous time. We see how the equation can be used to find the Fokker-Planck equation and how we can derive a mean-field set of partial differential equations to describe the temporal evolution of randomly connected balanced networks. The Fokker-Planck formalism allows us to analytically solve systems which would otherwise be intractable. This method is often used in theoretical neuroscience and it relies on the central limit theorem as well as the diffusion approximation, both of which will be further discussed in the preliminaries in Chapter 3. The reason we study the Fokker-Planck equation and its derivation in detail is that it is really a seminal equation in theoretical neuroscience and indeed very widely used both on the level of populations and infinite networks as well as smaller – even single cell – models. In fact, for many scientists in this discipline the term mean-field often implies the use of this equation. Of course this approach comes with its limitations which we will be addressing further in Chapters 5 and 6.

In Chapter 5 we see how the discussed mathematical methods can be applied to theoretical neuroscience. Here we take a look at three different models that make use of the mean-field approach and compare both their mathematical and biological properties. The models were chosen based on how they differ from one another. The first model is relatively simple and is based on the Fokker-Planck formalism. The Fokker-Planck approach, albeit useful and often used, has its drawbacks as previously mentioned. Using this approach requires some simplifying assumptions about the network behaviour and must thus compromise its accuracy for the ease of solving and simulating the system. The second model tries to combat these limitations by performing a change of coordinates in order to bypass the Fokker-Planck formalisms altogether. Because of this we can avoid making the diffusion approximation allowing us to retain a somewhat richer repertoire of network dynamics. Finally, the third model offers a solution to a problem which neither of the previous two can overcome. That is, sensory information does not travel instantaneously from neuron to neuron but in actuality some information time delay is always present. This can be accounted

for by building a coupled system consisting of both the single point-like neuron and a connective dendritic compartment with length and a diameter, providing us with more biologically relevant dynamics. The dendrite part of the equation can be modelled using the cable equation that will be explained in Section 3.5. The conclusions of the comparison of these models can be found in Chapter 6.

2 Mathematical models in neuroscience

In order to discuss mathematical modelling in neuroscience we need to first understand what neural cells are and how they can be described mathematically. Neurons are specialised brain cells, responsible for generating and propagating action potentials, the electrical signals responsible for sensory information transfer in the brain. In this thesis we concentrate on the mesoscopic level, that is, we are interested in models of populations of neurons. As the biological complexities of neuronal cells are not the main topic of this thesis, we will discuss the neuron and its features from a mathematical point of view and only briefly describe the biological structure and function of the cell itself.

2.1 The biology of a neuron

In general, neurons are thought to consist of three main components; a soma, an axon, and a dendritic tree. Simply put, the soma is the cell body where all of the vital cell functions take place, the axon is a long cable-like structure that carries the electrical impulse from the soma to other cells and the dendrites form a thinner branching network of cables that carry the electrical impulse toward the soma.. The input and output of the cell are the current it receives from other cells and the signal that it then sends forward, respectively. Crudely, one could say that the dendrites are where the cell receives its input and the axon then funnels the output forward to the next connected cell. This, of course, is not always the case but for the sake of simplicity it is enough to understand the models in this thesis. The structure of a real biological neuron is shown in Figure 2.1.

2.1.1 Properties of a neuron

The inputs of surrounding cells and the output to other cells are received and carried out through synapses between the dendrites and the axon. The cell generating the action potential is called the presynaptic cell, and the one receiving the signal is then called a postsynaptic cell.

The action potential itself is the most important feature of the neuron when it comes to the types of models considered in this thesis. The action potential, that being the electrical impulse generated in the neuron, arises from ions flowing through various ion channels located on the cell surface. These channels respond to voltage changes in both the cell and the extracellular space around it. The membrane potential of a given neuron is the difference in electrical potential between the inside and the outside of the cell and is mediated by the

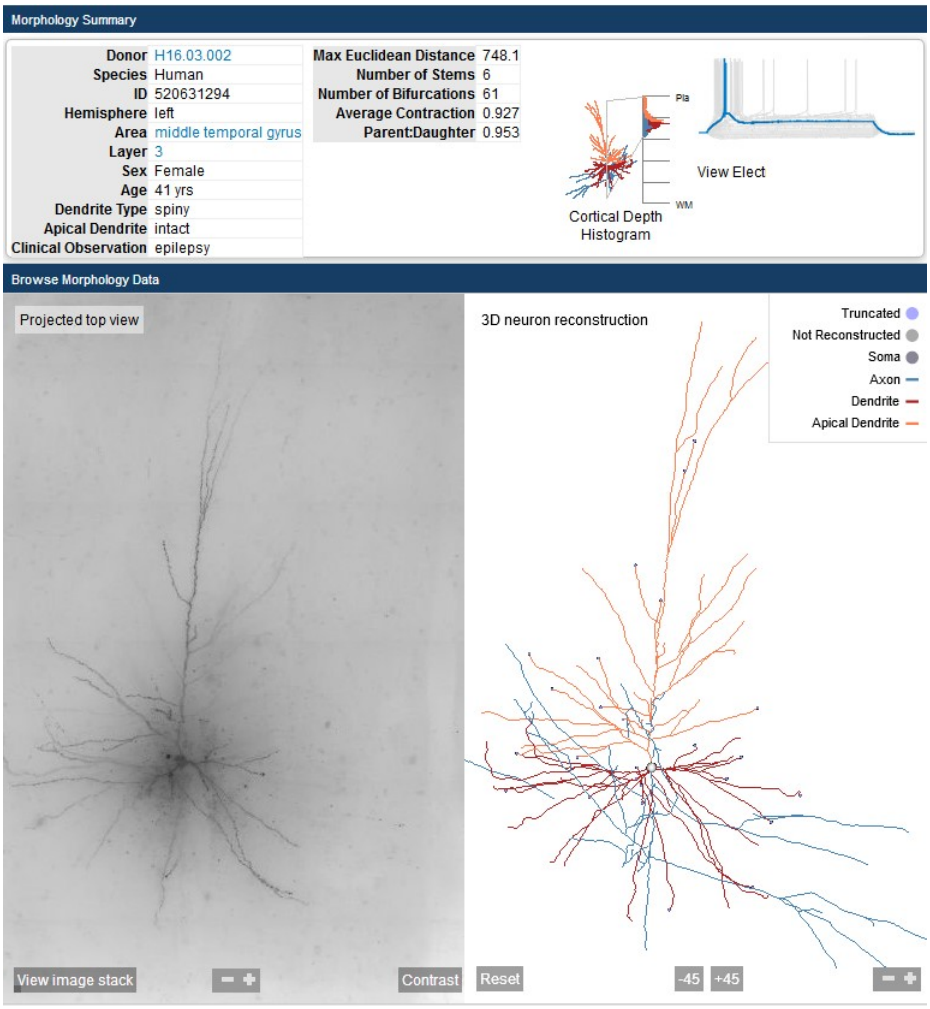

Figure 2.1: A pyramidal neuron from a 41-year-old female with epilepsy. Image from [1].

flow of ions in both directions. This ionic flow depends on the concentration gradients of the ions as well as ion pumps embedded into the cell membrane. These pumps influence the membrane potential by pumping ions of opposite charges either out of or into the neuron. The predominant ion pumps on neuronal membranes mediate the flow of sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), and chloride (Cl^-). When positively charged ions flow out of the cell, or conversely when negatively charged ions flow into the cell, the current created renders the membrane potential of the neuron more negative. This is considered an outward current flow, as the direction of the positive ions is from the cell to its extracellular space. This process is called hyperpolarisation. On the other hand, when the current flows into the cell making the membrane potential less negative, the process is called depolarisation. In this case positive ions flow in or negative ions flow out generating an inward current. The flow of these ions is governed both by the permeability of the cell membrane,

meaning the ease with which particular ions can travel through the channels on the cell surface, as well as by the charges on both sides of the membrane. This results in an *electrochemical* gradient, as the ions try to reach their *equilibrium potential*, at which the ion flow in balances with the flow out. This equilibrium voltage, or *reversal potential*, for each ion species can be calculated using the *Nernst equation*

$$E = \frac{V_T}{z} \ln\left(\frac{[ion]_{out}}{[ion]_{in}}\right), \tag{2.1}$$

where E is the equilibrium potential, $V_T = \frac{RT}{F}$ is the potential difference across the membrane, R, T, and F are the universal gas constant, temperature in Kelvin and Faraday constant, respectively. Furthermore z stand for the charge of the ion species, and $[ion]_{out}$ and $[ion]_{in}$ are the concentrations of the specific ions on the outside and inside of the cell. This equilibrium potential is also known as the *Nernst potential* and tells us at which voltage the flow of a specific ion species is at equilibrium, meaning that a slight change in either way causes the direction of the flow to be reversed. This means that the flow of any given ion species into our out of the cell will change so that they will flow into the opposite direction.[2]

Sufficient depolarisation leads to the membrane potential hitting a specific *threshold*, further driving a positive feedback process that initiates the generation of an *action potential*, also known as a *spike*, in the cell soma. Each time the cell *fires*, meaning that it generates an action potential, it has to go through a period of time when it is virtually incapable of generating another spike. This period lasts for a few milliseconds and is called the *absolute refractory period*. For a few milliseconds after the absolute refractory period it will be more difficult to initiate an action potential, until the membrane potential returns to its original resting value. This is called the *relative* refractory period. The transmission of sensory information between neurons happens through sequences of these spikes, and the relayed message depends on the temporal pattern and timing of those spikes. [2]

2.1.2 Neuronal networks

In the brain the synaptic connections between single cells form a network of interconnected neurons. The chemical connections between these neuronal cells are formed between the axons of the presynaptic and the cell membranes of the postsynaptic neurons. The signal passing from one neuron to another is the action potential, or spike, as mentioned above. One spike travelling from a cell to another usually causes the postsynaptic neuron to fire which again causes a spike in the next neuron and so on. This results in synchronous firing behaviour in neurons in a network.

When modelling such networks it is important to take excitatory and inhibitory interactions between different types of neurons into account. In network models this is usually done by adding weights to the connections between individual neurons if the population. Whereas biological neuronal networks can vary in size anywhere from dozens to thousands to million of neurons, model networks tend to be scaled down to smaller populations in order to increase the computational efficiency. [11] The mean-field approach does not require such down-scaling but is instead able to describe the behaviour of a large – even theoretically infinite – network. This is one of the main motivations behind using this type of approach.

2.2 Representing the neuron mathematically

Mathematical models in neuroscience normally differ mostly in terms of the number of equations and parameters used, multi-dimensional models being more biologically accurate and those with low dimensions being computationally less expensive [10]. In this section we first see how the complex biology behind the neuron can be reduced to a system of differential equations and then we introduce three different mathematical representations for a neuron, each portraying a different level of complexity. This will give the reader an idea of the spectrum of available models in terms of biological accuracy versus computational burden. The first and most important model we look at is the *Hodgkin-Huxley* neuron [6] which is the most biophysically accurate of the three. Subsequently we introduce a very simple neuron model, the *leaky-integrate-and-fire neuron* [10], and lastly the *Izhikevich neuron* [9] which has been formulated by combining the two aforementioned representations.

2.2.1 Resistor-capacitor circuit representation of a neuron

The neuron can be thought of as a relatively simple resistor-capacitor (RC) circuit, where the cell membrane acts as a capacitor, the ion channels as resistors, and the electrochemical gradient between the inside and outside of the neuron functions like a battery. This simplification is pictured in Figure 2.2.

The capacitor consists of two conductive regions, here the extra- and intracellular spaces, with a non-conductive separation in the middle, the cell membrane. When a conductive region acquires a charge it produces a current flowing from one region to the other, where the current is given by $I(t) = C\frac{dV}{dt}$. C stands for the capacitance and V for the potential.

With this representation we can now calculate the time constant τ that indicates the amount of time that it takes for the membrane to reach its steady state value after a change in voltage across it has occurred. We get τ using $\tau = RC$. [3]

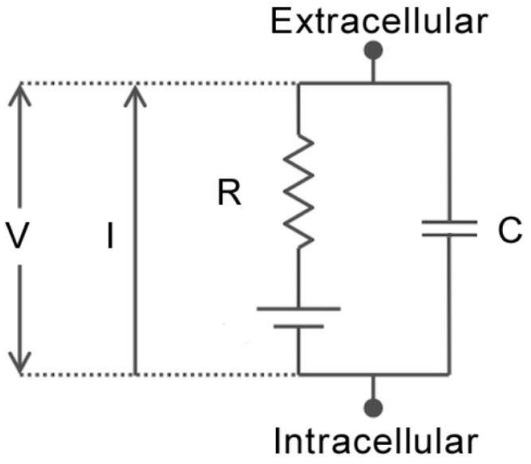

Figure 2.2: A neuron depicted as an RC-circuit. Image from [4].

2.2.2 The Hodgkin-Huxley model

One of the most frequently used single neuron models is the Hodgkin-Huxley (HH) model [6] of a squid giant axon derived in the 1950's by the two scientists, Alan Hodgkin and Andrew Huxley. Incorporated into the model are three different types of ion current; sodium, potassium, and a leak current that mostly consist of chloride ions. Here the cell membrane acts as a capacitor as explained above and all of the different types of ion channels have their own resistance values. The resistance for the leak current is fixed, whereas for the sodium and potassium channels it may significantly vary based on the proportions of open versus closed channels. Typically the resistance is not incorporated into the model as such, but as the conductance which is the reciprocal of the resistance. Since the different ion types have unique Nernst potentials as well, the channels also have their own reverse potentials. This slightly more complicated RC-circuit can be found in Figure 2.3.

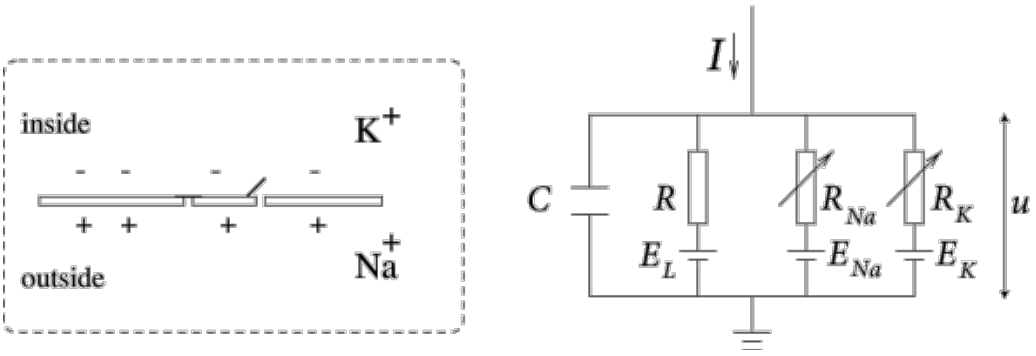

Figure 2.3: Schematic representation of a Hodgkin-Huxley neuron. Image from [8].

Because the electric charge is conserved on the membrane we can split the

incoming current $I(t)$ into the capacitive current $I_C(t)$ and the currents passing through the three different ion channels so that we arrive at the following expression

$$I(t) = I_C(t) + \sum_k I_k(t), \tag{2.2}$$

where k runs through the sodium, potassium, and leak channels. Because we get the capacitance by dividing the charge by the voltage across the capacitor, $C = \frac{q}{V}$, we find the charging current by differentiating the voltage with respect to time and multiplying by the capacitance; $I_C = C\frac{dV}{dt}$. Substituting the current $I(t)$ into Equation (2.2) we get

$$C\frac{dV(t)}{dt} = -\sum_k I_k(t) + I(t). \tag{2.3}$$

Here $V(t)$ is the membrane potential and I_k the ionic currents flowing through the membrane. The sum of these ionic currents can be found using the following equation

$$\begin{aligned}\sum_k I_k(t) &= g_{Na}(t)m^3(t)h(V(t) - E_{Na}) \\ &+ g_K(t)n^4(t)(V(t) - E_K) + h(t)g_L(V(t) - E_L),\end{aligned} \tag{2.4}$$

where $m(t), n(t)$, and $h(t)$ are the activation and inactivation variables, that is, the probabilities of the different ion channels being open at any given time. Here $g_{Na}(t), g_K(t)$, and $g_L(t)$ are the maximum conductances of the Na^+ and K^+ channels, as well as the leaky ion current, and E_{Na}, E_K, and E_L are the equilibrium potentials of those channels, respectively.

To account for the dynamics of this system we need to define the $m(t), n(t)$, and $h(t)$ terms more exactly. They are given by the following differential equations

$$\frac{dm(t)}{dt} = -\frac{1}{\tau_m(V(t))}[m(t) - m_0(V(t))], \tag{2.5}$$

$$\frac{dn(t)}{dt} = -\frac{1}{\tau_n(V(t))}[n(t) - n_0(V(t))], \text{ and} \tag{2.6}$$

$$\frac{dh(t)}{dt} = -\frac{1}{\tau_h(V(t))}[h(t) - h_0(V(t))]. \tag{2.7}$$

where τ_m, τ_n, and τ_h are the time constants with which m, n, and h approach $m_0(V(t)), n_0(V(t))$, and $h_0(V(t))$ for a fixed voltage $V(t)$. Now, to understand the action potential generation we must first pay attention to the fact that when $V(t)$ increases, so does m_0, whilst n_0 and h_0 decrease. This happens because when $V(t)$ grows more positive, the membrane depolarises, increasing the

likelihood of sodium channel opening and decreasing the chances of potassium and chloride channel opening. The opening of more sodium channels further raises the membrane potential in a positive feedback loop that – when large enough – causes the cell to fire an action potential, as described in Section 2.1. When the membrane potential reaches the reversal potential E_{Na} the increase in voltage comes to a halt.[8]

The Hodgkin-Huxley model represents the more biologically accurate end of the spectrum of available neuron models. This means that it incorporates a significant amount of detail and is thus clearly computationally more challenging than some of the other models available. Next we are going to look at one of the most often used simplified neuron models to see how the neuron can be represented in less detail but still retaining its biologically relevant properties.

The Hodgkin-Huxley model is a deterministic one, but in reality the ion channels on the surface of the neuron open and close stochastically [7]. Mathematically this can be easily fixed by adding a noise term.

2.2.3 The Leaky Integrate-and-Fire model

Describing spiking behaviour of neurons is easy with the use of so-called *point neuron models*. In mean-field modelling the most widely used point neuron model is the relatively simple leaky integrate-and-fire (LIF) neuron. The LIF model can also be modified by adding more complex functionalities in order to achieve a more realistic – yet rather simplistic – model with more dynamic features than the regular LIF has to offer.

The leaky integrate-and-fire neuron is described by its membrane potential V and includes the following functional features; the membrane potentials for rest, a spiking threshold, and a reset after the spike, as well as a membrane time constant τ, and a refractory time period that the neuron stays inactive after a spike. These concepts are an important part of understanding neuronal modelling and they will come up throughout this thesis. The LIF model is usually of the form

$$C\frac{dV(t)}{dt} = -g_L(t)(V(t) - E_L) + \sum_k I_k(t), \tag{2.8}$$

where C is the capacitance of the neuron, $g_L(t)$ its leak conductance, E_L the leak reversal potential, and $\sum_k I_k(t)$ all of the synaptic inputs summed together. This is often normalised with respect to the leak conductance, yielding

$$\tau_m\frac{dV(t)}{dt} = -(V(t) - E_L) + \sum I_{syn}(t), \tag{2.9}$$

where τ_m is the membrane time constant $\frac{C}{g_L(t)}$ and I_{syn} is the synaptic inputs given as units of voltage, where $I_{syn} = \frac{I_k(t)}{g_L(t)}$.

The basic principle of the leaky integrate-and-fire model is based on its membrane potential. When a certain threshold value θ is reached a spike is emitted and the membrane potential $V(t)$ resets to the reset potential V_r after an absolute refractory period τ_{rp}. When the input current in the model is constant, the model exhibits a clear threshold for the generation of the action potentials but this is not very realistic. The clarity of the threshold means that when the membrane potential reaches θ it resets instantaneously. In reality the rising membrane potential causes the potassium and chloride channels to open, gradually lowering V_m back to its reverse value. Realistic input currents are of course stochastic and thus harder to analyse. This is why we make the assumption that they are rather deterministic, giving us spike trains that are easier to analyse. Because of this some simplifications are often necessary. [10]

Due to being a gross simplification, the LIF model neglects several important neuronal properties. For example it cannot account for different spiking patterns, much less neuronal bursting behaviour nor *adaptation*. LIF represents the computationally most efficient end of the spectrum of available mathematical models for neurons. [8]

2.2.4 The Izhikevich model

The Simple Model of Spiking Neurons by Eugene M. Izhikevich [9] combines the Hodgkin-Huxley -type biologically accurate dynamics with the ease of computation of the integrate-and-fire-type neurons. It is capable of reproducing both spiking and bursting behaviour of different types of known cortical neurons as well as simulating networks of tens of thousands of spiking neurons in real time.

The *Izhikevich model* reduces Hodgkin-Huxley-type neurons to a relatively simple two-dimensional system of ODEs

$$\frac{dV(t)}{dt} = 0.04V(t)^2 + 5V(t) + 140 - U(t) + I(t) \tag{2.10}$$

$$\frac{dU(t)}{dt} = a(bV(t) - U(t)), \tag{2.11}$$

where $V(t)$ represents the membrane potential, $U(t)$ the recovery variable accounting for the activation of the potassium (K^+) channels and inactivation of sodium (Na^+) channels. Parameters $V(t)$ and $U(t)$ are dimensionless variables. Here a, and b are dimensionless parameters the model depends on to produce spiking and bursting behaviour. Parameters a, b, and d describe the time-scale, sensitivity, and after-spike reset of the recovery variable $U(t)$, respectively, whereas c gives the after-spike reset value of the membrane potential $V(t)$. $I(t)$ is the synaptic and injected currents. The after-spike resetting properties of the model are given by the following condition

$$\text{if } V(t) \geq 30\text{mV, then } \begin{cases} V(t) = c \\ U(t) = U(t) + d, \end{cases} \tag{2.12}$$

where c, and d are also dimensionless variables responsible for inducing varied spiking behaviours. Networks built from these Izhikevich neurons are capable of reproducing collective dynamics and rhythms similar to those found in *in vivo* mammalian cortices due to the biophysical accuracy it gets from the Hodgkin-Huxley formalism. Still, being a simplified model it is extremely inexpensive computationally allowing for fast real time simulation and analysis of large networks.

2.3 Mean-field theory and model neurons

Neuronal dynamics result from the interaction of neurons on different biophysical levels ranging from the flow of ions on the macroscopic to neural populations on the mesoscopic level. Similar dynamical problems have been well-studied in the field of particle physics and these methods can be applied to theoretical neuroscience. Originally the mean-field formalism was developed to describe the average spin of electrons but it can be similarly utilised in describing neuronal interactions. The Hodgkin-Huxley model discussed in Section 2.2.2 is a great example of this. The Hodgkin-Huxley model derived from the real physical giant axon of a squid uses multiple equations to describe the synaptic transmission between neurons. This behaviour, even though it is rather well described by the laws of physics, is still not quite as straightforward as the electron spin problem. First of all the inter-cellular behaviour is not symmetric but changes with time depending on the pre- and postsynaptic stimuli, there is no clear conservation of energy or momentum, and there is no natural probability distribution to describe the dynamics.[13]

What the mean-field approach really allows us to do is to take a single neuron model and generalise it to a population of neurons in such a way that we can represent the whole population in terms of the single neuron model by assuming that the behaviour of each neuron in the population is the same. This is possible through the central limit theorem discussed in Section 3.4.1, because when the size of the population tends to infinity the state of each neuron tends to a Gaussian distribution. Given the fact that in large populations of neurons their behaviour becomes mostly asynchronous this is a logical assumption to make. Now the distribution of neuronal states is the same for each cell in our population, thus allowing us to represent all of the neurons using just one equation. In this case we scale the inter-neuronal interactions by $\frac{1}{N}$, leaving us with a deterministic system.

So the mean-field approach allows us to represent a large population of spiking neurons in terms of a single distribution function. This function will give us information on the time evolution of the probability density of the neuronal population, meaning that we acquire a description for the likely distribution of the neuronal states at any given time. The state space depends on the model used but in general the sate of a neuron tells us whether the cell is currently spiking or not. This state distribution can be reduced to a one-body problem by

introducing a single variable describing the mean firing rate of the population. The distribution of probable neuronal states can also be represented by a set of scalars equivalent to the moments of the distribution, that being the mean and the variance.

When using the mean-field approach one neglects random fluctuations by means of replacing the fluctuating variables with their mean averages. This approximation loses some information but ensures that the system dynamics converge to a stationary attractor consistent with the steady-state dynamics of the underlying system. [13]

Generally the mean-field models used in neuroscience can be classified into one of two distinct types; *neural mass* and *neural field* models. The two types differ from each other mainly in the way they describe the time evolution of neural activity. Neural field models depict the evolution of a given activity measure over both *space and time*, whereas neural mass models can characterise the activity of the system over time only. In the latter case it is assumed that the neurons in the population are located in very close proximity of each other. [5]

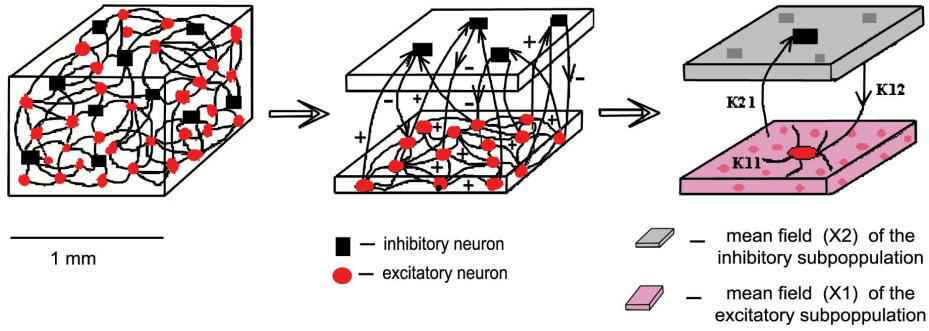

Figure 2.4: This figure depicts how a group of neurons can be divided into statistically similar populations which are then represented by their respective average behaviour. Image from [12].

To conclude; in order to describe the spiking behaviour of a population of neurons, the mean-field approach uses a simplified spiking neuron model, the idea of which is then extended to the whole population. This is based on the fact that when the population is large enough the behaviour of any of the neurons in the network can be described by the mean average of the whole population, effectively leaving us with just one (partial) differential equation for the average behaviour. [10]

Often statistically similar neurons are grouped together into populations of e.g. inhibitory and excitatory neurons. Then these populations are described by the average of the behaviour of the respective population. This is schematically shown in Figure 2.4.

In the three models we will concentrate on in this thesis we see different types of single neuron models on which we apply the mean-field approach. The

simplest of these is the LIF model that describes the spiking behaviour of a neuron. Then we look at the geometry based method of Marc de Kamps et al. [27] which can be used on more detailed models like the Hodgkin-Huxley or the Izhikevich neuron. The last of the three models studied in this thesis incorporates a dendritic compartment into the system. It uses the noisy LIF neuron, meaning that a noise term is added to the existing model.

3 Preliminaries

In this chapter we present the reader with some definitions and theorems that are essential for understanding this thesis.

3.1 Probability distributions

As all of the models studied in this thesis are based on the time evolution of probability distributions we need to get familiar with relevant concepts. These definitions and theorems can be found in [14] and [15]. We assume that the reader has a rudimentary knowledge of the basic concepts of probability theory.

Definition 3.1. [14] Let S be a set and let $\mathcal{P} = \{A_i\}_{i=1}^m$ be a collection of subsets of S. The collection $\mathcal{P}$ is called a *partition of* S if

- $S = \bigcup_{i=1}^m A_i$
- $A_i \cap A_j = \emptyset$ for $i \neq j$.

Theorem 3.1 (Bayes' theorem)**.** *[14] If the events $\{B_i\}_{i=1}^m$ constitute a partition of the sample space S and $P(B_i) \neq \emptyset$ for $i = 1, 2, \ldots, m$, then for any event A in S*

$$P(A) = \sum_{i=1}^{m} P(B_i)P(A|B_i). \tag{3.1}$$

Definition 3.2. [14] Let R_X be the space of a random variable X. The function $f : R_X \to \mathbb{R}$ defined by

$$f(x) = P(X = x)$$

is called the *probability density function* of X. If X is a continuous random variable then $f : \mathbb{R} \to [0, \infty)$ is a continuous function such that for every set of real numbers A

$$P(X \in A) = \int_A f(x)dx.$$

and

$$\int_{-\infty}^{\infty} f(x)dx = 1.$$

Definition 3.3. [14] The nth *moment* about the origin of a continuous random variable X, as denoted by $E(X^n)$, is defined to be

$$E(X^n) = \int_{-\infty}^{\infty} x^n f(x)dx$$

for $n = 1, 2, 3, \ldots$, provided that the integral on the right-hand side converges absolutely. The first moment about the origin $E(X)$ is the *mean* and the second moment $E(X^2)$ is the *variance* of the random variable X.

Definition 3.4. [14] Let X be a random variable whose probability density function is $f(x)$. A real-valued function $M : \mathbb{R} \to \mathbb{R}$ defined by

$$M(t) = E(e^{tx})$$

is called the *moment generating function* of X if this expected value exists for all t in interval $-h \leq t \leq h$ for some $h \geq 0$. For a continuous random variable we obtain the following representation for the moment generating function

$$M(t) = \int_{-\infty}^{\infty} e^{tx} f(x) dx.$$

Theorem 3.2. *[14] Let $M(t)$ be the moment generating function of the random variable X. If*

$$M(t) = a_0 + a_1 t + a_2 t^2 + \cdots + a_n t^n + \cdots$$

is the Taylor series expansion of $M(t)$, then

$$E(X^n) = (n!)a_n$$

for all $n \in \mathbb{N}$

Definition 3.5. [14] A random variable X is said to have a *Poisson distribution* if its probability density function is given by

$$f(x) = \frac{e^{-\lambda}\lambda^x}{x!}, \quad x = 0, 1, 2, \ldots,$$

where $0 < \lambda < \infty$ is a parameter.

Definition 3.6. [14] A random variable X is said to have a *normal distribution* if its probability density function is given by

$$f(x) = \frac{1}{\sigma\sqrt{2\pi}} e^{-\frac{1}{2}(\frac{x-\mu}{\sigma})^2}, \quad -\infty < x < \infty,$$

where $-\infty < \mu < \infty$ and $0 < \sigma < \infty$ are the mean and the variance.

Definition 3.7. [14] Let X and Y be continuous random variables. An integrable function $f : \mathbb{R}^2 \to \mathbb{R}$ is called a *joint probability density function* $f(x, y)$, if

- for all $(x, y) \in \mathbb{R}^2$, $f(x, y) \geq 0$, and
- $\int_{-\infty}^{\infty} \int_{-\infty}^{\infty} f(x, y) dx dy = 1.$

Definition 3.8. [14] Let (X, Y) be a continuous bivariate random variable. Let $f(x, y)$ be the joint probability density function of X and Y. The function

$$f_1(x) = \int_{-\infty}^{\infty} f(x, y)dy$$

is called the *marginal probability density function* of X. Similarly, the function

$$f_2(y) = \int_{-\infty}^{\infty} f(x, y)dx$$

is called the *marginal probability density function* of Y.

Definition 3.9. [14] Let X and Y be any two random variables with joint density $f(x, y)$ and marginals $f_1(x)$ and $f_2(y)$. The *conditional probability function* g of X given the event $Y = y$ is defined as

$$g(x|y) = \frac{f(x, y)}{f_2(y)}, \qquad \forall y \text{ such that } f_2(y) > 0.$$

Definition 3.10. [14] The conditional mean of a continuous random variable X given $Y = y$ is defined as

$$\mu_{X|y} = E(X|y),$$

where

$$E(X|y) = \int_{-\infty}^{\infty} xg(x|y)dx.$$

Definition 3.11. [14] Let $X_1, X_2, \ldots, X_n$ be a random sample from a population X. Let $p(x; \theta)$ be the probability distribution of X where θ is a parameter. Now a function T, such that

$$T = T(X_1, X_2, \ldots, X_n)$$

is called a *statistic*. The statistic is by definition free of the parameter θ. The probability distribution for the statistic T is called the *sampling distribution*.

3.2 Solving Partial Differential Equations

If a PDE cannot be solved outright we need to resort to approximating and estimating the solutions as best we can. These methods include numerical analysis and deducing the properties of the solutions.[16] Here we will give the reader a quick overview of the techniques we use to solve PDEs in this thesis.

Definition 3.12. [16] A *Dirichlet boundary value problem* is such where the value of the solution is given by

$$u = g \text{ on } \partial\Omega.$$

A *Neumann boundary value problem* is one where the outward normal derivative is given by

$$\frac{\partial u}{\partial \nu} = g \text{ on } \partial\Omega,$$

where $\frac{\partial u}{\partial \nu} = \nabla u \cdot \nu$ is the outward normal derivative and ν the outward unit normal vector.

Definition 3.13. [17] The *Fourier series* is an infinite series of the form

$$f(x) = \frac{a_0}{2} + \sum_{n=1}^{\infty} \left[a_n \cos\left(\frac{n\pi x}{L}\right) + b_n \sin\left(\frac{n\pi x}{L}\right) \right],$$

where $n \in \mathbb{Z}_+$, $L > 0$ and $L \in \mathbb{R}$. Here a_n and b_n are the *Fourier coefficients*. All the terms in the Fourier series expression are periodic of $2L$ which means that the Fourier series itself is also periodic of $2L$ and so

$$f(x + 2L) = f(x).$$

Definition 3.14. [17] The *Fourier coefficients* a_n and b_n can be found using the following *orthogonality integrals*

$$\int_{-L}^{L} \cos\left(\frac{n\pi x}{L}\right) \cos\left(\frac{m\pi x}{L}\right) = \begin{cases} 0, & \text{if } n \neq m \\ L, & \text{if } n = m \end{cases}$$

$$\int_{-L}^{L} \sin\left(\frac{n\pi x}{L}\right) \sin\left(\frac{m\pi x}{L}\right) = \begin{cases} 0, & \text{if } n \neq m \\ L, & \text{if } n = m \end{cases}$$

$$\int_{-L}^{L} \sin\left(\frac{n\pi x}{L}\right) \cos\left(\frac{m\pi x}{L}\right) = 0 \qquad \forall m, n \in \mathbb{Z}_+.$$

Using the orthogonality integrals and trigonometric identities, if we multiply the Fourier series on both sides with $\cos(\frac{m\pi x}{L})$ we have for all $m \in \mathbb{Z}_+$

$$\cos\left(\frac{m\pi x}{L}\right) \int_{-L}^{L} f(x)dx = \cos\left(\frac{m\pi x}{L}\right) \int_{-L}^{L} \left[\frac{a_0}{2} + \sum_{n=1}^{\infty} a_n \cos\left(\frac{n\pi x}{L}\right) + b_n \sin\left(\frac{n\pi x}{L}\right) \right] dx$$

$$\int_{-L}^{L} \cos\left(\frac{m\pi x}{L}\right) f(x)dx = \frac{a_0}{2} \int_{-L}^{L} \cos\left(\frac{m\pi x}{L}\right) + \sum_{n=1}^{\infty} \left[a_n \int_{-L}^{L} \cos\left(\frac{n\pi x}{L}\right) \cos\left(\frac{m\pi x}{L}\right) dx \right.$$

$$\left. + b_n \int_{-L}^{L} \sin\left(\frac{n\pi x}{L}\right) \cos\left(\frac{m\pi x}{L}\right) dx \right].$$

Using the orthogonalities the first and last term equal to zero, yielding

$$\int_{-L}^{L} f(x)\cos\left(\frac{m\pi x}{L}\right)dx = \sum_{n=1}^{\infty} a_n \int_{-L}^{L} \cos\left(\frac{n\pi x}{L}\right)\cos\left(\frac{m\pi x}{L}\right)dx$$
$$= a_m \int_{-L}^{L} \cos^2\left(\frac{m\pi x}{L}\right)dx = a_m L$$

as the integral is non-zero only when $n = m$. This leaves us with the formula for the coefficient a_n

$$a_n = \frac{1}{L}\int_{-L}^{L} \cos\left(\frac{n\pi x}{L}\right)f(x)dx. \tag{3.2}$$

Similarly this can be done to derive

$$a_0 = \frac{1}{L}\int_{-L}^{L} f(x)dx$$

and

$$b_n = \frac{1}{L}\int_{-L}^{L} \sin\left(\frac{n\pi x}{L}\right)f(x)dx.$$

Theorem 3.3. *[17] If a function $f(x)$ and its first derivative $f'(x)$ are continuous or piecewise continuous on the interval $[-L, L]$ and if $f(x)$ is periodic with period $2L$, The Fourier series of $f(x)$ will converge with coefficients*

$$a_n = \frac{1}{L}\int_{-L}^{L} \cos\left(\frac{n\pi x}{L}\right)f(x)dx$$

and

$$b_n = \frac{1}{L}\int_{-L}^{L} \sin\left(\frac{n\pi x}{L}\right)f(x)dx$$

Remark 1. *In this thesis we are interested in functions that are discontinuous only at sharp jumps. These types of functions are used to describe the resetting behaviour of the membrane potential modelled in theoretical neuroscience. At such a jump, the Fourier series converges to the average value, i.e.*

$$S_N(x) \to \lim_{\varepsilon\to 0} \frac{f(x+\varepsilon) + f(x-\varepsilon)}{2},$$

where $\varepsilon > 0$.

Definition 3.15. [17] The Fourier series can be expressed in terms of complex variables as

$$\begin{aligned} e^{ix} &= \cos(x) + i\sin(x), \\ \cos(x) &= \frac{e^{ix} + e^{-ix}}{2} \\ \sin(x) &= \frac{e^{ix} - e^{-ix}}{2i}. \end{aligned}$$

With this we can express the Fourier series in its *complex form*

$$f(x) = \sum_{-\infty}^{\infty} c_n e^{\frac{in\pi x}{L}}.$$

Definition 3.16. [17] A function $h(t) : [-L, L] \to \mathbb{R}$ is said to be *Lebesgue integrable*, denoted by $h \in L^1$, if it satisfies

$$\int_{-\infty}^{\infty} |h(t)|dt < \infty,$$

and *square integrable*, denoted by $h \in L^2$, if it in turn satisfies

$$\int_{-\infty}^{\infty} |h(t)|^2(t)dt < \infty.$$

Definition 3.17. [17] Let $h(t) : [-L, L] \to \mathbb{R}$ be a function such that $h \in L^1$. Now we can find the *Fourier transform* of $h(t)$

$$\mathcal{F}[h(t)] = H(f) = \int_{-\infty}^{\infty} h(t)e^{-2\pi ift}dt,$$

and the *inverse Fourier transform* of $H(t)$

$$\mathcal{F}^{-1}[H(f)] = h(t) = \int_{-\infty}^{\infty} H(f)e^{2\pi ift}df.$$

An aperiodic function can always be represented with a unique Fourier transform and for any function the transform and its inverse will always uniquely determine the other. Moreover, the Fourier transform can be extended for all square integrable functions $g \in L^2$.

Theorem 3.4. *[16] Let $\partial\Omega \in \mathcal{C}^1$, $u \in \mathcal{C}^2(\bar{\Omega})$. If u solves*

$$\begin{cases} -\Delta u = f & \text{in } \Omega \\ u = g & \text{on } \partial\Omega, \end{cases}$$

then

$$u(x) = -\int_{\partial\Omega} g(y)\frac{\partial G}{\partial \nu}(x, y)dS(y) + \int_{\Omega} f(y)G(x, y)dy,$$

where G is the Green function, and $S(y)$ the oriented surface element.

Remark 2. *[16] It is useful to remember the* integration by parts formula

$$\int_U u_{x_i} v dx = -\int_U u v_{x_i} dx + \int_{\partial U} u v \nu^i dS$$

for $i \in 1, \ldots, n$. Here again ν is the outward pointing unit normal vector to the boundary.

3.3 Stochastic processes

In this section we will look at Brownian motion and how it is defined. We shall see how Einstein originally described Brownian motion and how it relates to the Chapman-Kolmogorov equation and the Fokker-Planck equation that will be presented in Chapter 4. As the latter equation gives us the time evolution of a probability density function of the positions of particles following a stochastic differential equation, we need to be aware of the underlying stochastic processes that affect the evolution of the probability distribution.[18] In Chapter 4 we will derive both the master equation and the Fokker-Planck equation. First we will take a look at some basic properties of stochastic variables both in the single variable case and the multivariate case.

3.3.1 Single variable case

A random variable X is a quantity defined by the phase space $\{x\}$, and a probability distribution $P_X(x)$. We are dealing with continuous random variables here, but they could as well be discrete. The probability distribution is a non-negative function and

$$\int P_X(x) dx = 1, \tag{3.3}$$

as indicated in Definition 3.2.

3.3.2 Brownian motion

In order to understand Brownian motion, as described by Albert Einstein, we need to first look at a few definitions for stochastic variables.

Definition 3.18. [15] A (centred) *Gaussian space* is a closed linear subspace of $L^2(\Omega, \mathcal{F}, P)$ which contains only centred Gaussian variables. $L^2(\Omega, \mathcal{F}, P)$ is the space of *square-integrable intensity functions* $f : \Omega \to \mathcal{F}$, with intensity P.

Definition 3.19. [15] Let $(E, \mathcal{E})$ be a measure space, and let T be an arbitrary index set. A *stochastic process* (indexed by T) with values in E is a collection $(X_t)_{t \in T}$ of random variables with values in E. If the measure space $(E, \mathcal{E})$ is not specified, we will implicitly assume that $E = \mathbb{R}$ and $\mathcal{E} = \mathcal{B}(\mathbb{R})$ is the Borel σ-field on $\mathbb{R}$.

Definition 3.20. [15] Let $(E, \mathcal{E})$ be a measurable space, and let μ be a σ-finite measure on $(E, \mathcal{E})$. A *Gaussian white noise* with intensity μ is an isometry G from $L^2(E, \mathcal{E}, \mu)$ into a (centred) Gaussian space. Here $L^2(E, \mathcal{E}, \mu)$ is the space of square-integrable functions $f : E \to \mathcal{E}$ with intensity μ. Hence, if $f \in L^2(E, \mathcal{E}, \mu), G(f)$ is centred Gaussian with variance

$$E[G(f)^2] = |G(f)|^2_{L^2(\Omega,\mathcal{F},P)} = |f|^2_{L^2(E,\mathcal{E},\mu)} = \int f^2 d\mu.$$

If $f, g \in L^2(E, \mathcal{E}, \mu)$, the covariance of $G(f)$ and $G(g)$ is

$$E[G(f)G(g)] = \langle f, g \rangle_{L^2(E,\mathcal{E},\mu)} = \int fg d\mu.$$

3.3.3 From Gaussian noise to Brownian motion

When Einstein first described the concept of *Brownian motion* in 1905 he made two principal characterisations:

- the motion of the particles is caused by the frequent impacts between the liquid in which the particles are suspended and the particles themselves
- and the resultant motion is complicated enough to only be describable in probabilistic terms due to the frequent and statistically independent impacts.

Einstein reasoned that the motion of each individual particle must be independent of all of the other particles, as well as its own motion in different time steps. The movements of a single particle can be seen as independent processes when a time interval τ is introduced such that τ is the time between independent motions, where τ is very small but still large enough to separate the movements from each other.[20]
The formal definition of Brownian motion is the following:

Definition 3.21. [19] A standard *Brownian motion* is a stochastic process $W_{t\geq 0+}$ with properties

- $W_0 = 0$,
- with a probability 1, the function $t \to W_t$ is continuous in t,
- the process $W_{t\geq 0}$ has stationary, independent increments, and
- the increment $W_{t+s} - W_s$ has the normal $(0, t)$ distribution.

Let us now consider n particles suspended in a liquid. With our given time interval τ the x-coordinates of individual particles will change by a measure of

Δ which is unique for each particle. If dn is the number of particles moving between Δ and $\Delta + d\Delta$, we can express it as follows: $dn = n\phi(\Delta)d\Delta$, where

$$\int_{-\infty}^{\infty} \phi(\Delta)d\Delta = 1,$$

and ϕ is such that it is non-zero only when Δ is very small, and it satisfies the following condition: $\phi(-\Delta) = \phi(\Delta)$. If we restrict ourselves into a situation where the number of particles per a given unit of volume depends only on x and t, we can easily see how the diffusion coefficient depends on ϕ. So if $f(x,t)$ is the number of particles per unit volume, we can find the number of particles at time $t + \tau$ from the distribution of particles at time t. We find that the number of particles at time $t + \tau$ between points x and $x + dx$ is given by

$$f(x, t+\tau)dx = dx \int_{-\infty}^{\infty} f(x+\Delta, t)\phi(\Delta)d\Delta. \tag{3.4}$$

But as τ is very small we can assume that

$$f(x, t+\tau) = f(x,t) + \tau\frac{\partial f}{\partial t} \cdots .$$

Expanding $f(x + \Delta, t)$ in powers of Δ yields the series

$$f(x+\Delta, t) = f(x,t) + \Delta\frac{\partial f(x,t)}{\partial x} + \frac{\Delta^2}{2!}\frac{\partial^2 f(x,t)}{\partial x^2} + \cdots ,$$

which we can use under the integral in Equation (3.4) to obtain the following expression

$$\begin{aligned} f(x,t) + \tau\frac{\partial f(x,t)}{\partial t} = f(x,t)\int_{-\infty}^{\infty} \phi(\Delta)d\Delta + \frac{\partial f(x,t)}{\partial x}\int_{-\infty}^{\infty} \Delta\phi(\Delta)d\Delta \\ + \frac{\partial^2 f(x,t)}{\partial x^2}\int_{-\infty}^{\infty} \frac{\Delta^2}{2}\phi(\Delta)d\Delta + \cdots . \end{aligned} \tag{3.5}$$

Because $\int_{-\infty}^{\infty} \phi(\Delta)d\Delta = 1$, $f(x,t)\int_{-\infty}^{\infty} \phi(\Delta)d\Delta$ becomes $f(x,t)$, and the $f(x,t)$ on the left-hand-side cancels it out, leaving us with

$$\tau\frac{\partial f(x,t)}{\partial t} = \frac{\partial f(x,t)}{\partial x}\int_{-\infty}^{\infty} \Delta\phi(\Delta)d\Delta + \frac{\partial^2 f(x,t)}{\partial x^2}\int_{-\infty}^{\infty} \frac{\Delta^2}{2}\phi(\Delta)d\Delta + \cdots . \tag{3.6}$$

If we now note that $dn = n\phi(\Delta)d\Delta$ we have $\Delta\phi(\Delta)d\Delta = d\Delta$, giving us

$$\frac{\partial f(x,t)}{\partial x}\int_{-\infty}^{\infty} \Delta\phi(\Delta)d\Delta = \frac{\partial f(x,t)}{\partial x}\int_{-\infty}^{\infty} d\Delta = 0.$$

This leaves us with

$$\tau \frac{\partial f(x,t)}{\partial t} = \frac{\partial^2 f(x,t)}{\partial x^2} \int_{-\infty}^{\infty} \frac{\Delta^2}{2} \phi(\Delta) d\Delta. \tag{3.7}$$

Of the remaining terms each one is very small in comparison to the previous one. As

$$\int_{-\infty}^{\infty} \phi(\Delta) d\Delta = 1,$$

if we define D as

$$D = \frac{1}{\tau} \int_{-\infty}^{\infty} \frac{\Delta^2}{2} \phi(\Delta) d\Delta,$$

and assume the fourth and higher terms to be negligible, we are left with

$$\frac{\partial f(x,t)}{\partial t} = D \frac{\partial^2 f(x,t)}{\partial x^2}. \tag{3.8}$$

We can see that this is the partial differential equation describing diffusion, and here D is the diffusion coefficient. The original problem now clearly corresponds to a problem of diffusion from a single point, and its solution can be mathematically determined.

We can use the method of integral transform to solve the partial differential equation. First we introduce the space Fourier transform of $f(x,t)$ as well as its inverse

$$F(k,t) = \int_{-\infty}^{\infty} e^{-ikx} f(x,t) dx, \qquad f(x,t) = \frac{1}{2\pi} \int_{-\infty}^{\infty} e^{-ikx} F(k,t) dk, . \tag{3.9}$$

transforming the diffusion equation (3.8) into the simple form

$$\frac{\partial F}{\partial t} = -Dk^2 F \implies F(k,t) = F(k,0) e^{-Dk^2 t}. \tag{3.10}$$

When the initial condition $f(x,0) = \delta(x)$ is set, then the Fourier transform yields $F(x,0) = 1$. Now, when the inverse transform is taken in the k-space, we arrive at

$$\begin{aligned} f(x,t) &= \frac{1}{2\pi} \int e^{ikx} e^{-Dk^2 t} dk \\ &= \frac{e^{-(x^2/4D)t}}{2\pi} \int e^{-Dt(k - i(x/2D)t)^2} dk \\ &= \frac{e^{-(x^2/4D)t}}{\sqrt{\pi 4Dt}}. \end{aligned} \tag{3.11}$$

Equation (3.11) is now our solution to the original problem. With the help of this formula we can calculate the average displacement λ_x that a particle experiences in the direction of the x-axis

$$\lambda_x = \sqrt{\langle x^2 \rangle - \langle x_0^2 \rangle} = \sqrt{2Dt}. \tag{3.12}$$

This derivation by Einstein contains many concepts that will be useful throughout this thesis, the most important of which are the following three:

- The *Chapman-Kolmogorov equation* (3.4) tells us that the probability of a particle being at a certain point on the x-axis at time $t + \tau$ is found by multiplying the probability of being at $x + \Delta$ at time t by the sum of the probabilities of all displacements Δ from positions $x + \Delta$. We can make this assumption due to the independent nature of the displacements Δ, as it necessary to only know the initial position of the particle at time t. This is a property of all Markov processes, and will be discussed further in Section 4.1.1.
- The *Kramers-Moyal expansion* is then used to get from Equation (3.4) to the diffusion equation (3.8). We will take a closer look at this in Section 4.2.1.
- And finally we have the *Fokker-Planck equation*, of which the diffusion equation (3.8) is a special case. We will derive the Fokker-Planck equation in Chapter 4 and further discuss its properties in Section 4.2.

Definition 3.22. The *characteristic function* is defined by the average of e^{ikX}, where

$$G_X(k) = E(e^{ikX}) = \int e^{ikx} P_X(x) dx. \tag{3.13}$$

This is a *Fourier transform* of $P_X(x)$, and can be solved for the probability distribution

$$P_X(x) = \frac{1}{2\pi} \int_{-\infty}^{\infty} e^{-ikx} G_X(k) dk.$$

Let us denote the moments of the probability distribution by $\mu_m = E(X^m)$. Here the function $G_X(k)$ gives us an alternative way of describing the probability distribution. Extending the exponential function in Equation (3.13) and changing the order of terms gives us

$$G_X(k) = \sum_{m=0}^{\infty} \frac{(ik)^m}{m!} \int x^m P_X(x) dx = \sum_{m=0}^{\infty} \frac{(ik)^m}{m!} \mu_m. \tag{3.14}$$

Now the characteristic function of $P_X(x)$ is found to be $G_X(k)$, as

$$\mu_m = (-i)^m \frac{\partial^m}{\partial k^m} G_X(k)|_{k=0}. \tag{3.15}$$

Much like the moment generating function, the characteristic function completely defines the probability distribution. Still it can be more useful as as long as the characteristic function is a function of a real-valued argument it will always exist.

Definition 3.23. The *cumulants* κ_m are the coefficients of the expansion of the cumulant function $\ln G_X(k)$ in powers of ik

$$\ln G_X(k) = \sum_{m=1}^{\infty} \frac{(ik)^m}{m!} \kappa_m.$$

Using the above definition we find the relationship between the first four cumulants and the moments to be

$$\begin{aligned}
\kappa_1 &= \mu_1 \\
\kappa_2 &= \mu_2 - \mu_1^2 \\
\kappa_3 &= \mu_3 - 3\mu_2\mu_1 + 2\mu_1^3 \\
\kappa_4 &= \mu_4 - 4\mu_3\mu_1 - 3\mu_2^2 + 12\mu_2\mu_1^2 - 6\mu_1^4.
\end{aligned}$$

So the first cumulant corresponds with the first moment – corresponding to the mean – of the stochastic variable. There also exists a general expression for the cumulants which can be given in the terms of the determinant of a $m \times m$ matrix made of the moments $\{\mu_i \mid i = 1, \ldots, m\}$

$$\kappa_m = (-1)^{m-1} \begin{vmatrix}
\mu_1 & 1 & 0 & 0 & 0 & \cdots \\
\mu_2 & \mu_1 & 1 & 0 & 0 & \cdots \\
\mu_3 & \mu_2 & \binom{2}{1}\mu_1 & 1 & 0 & \cdots \\
\mu_4 & \mu_3 & \binom{3}{1}\mu_2 & \binom{3}{2}\mu_1 & 1 & \cdots \\
\mu_5 & \mu_4 & \binom{4}{1}\mu_3 & \binom{4}{2}\mu_2 & \binom{4}{3}\mu_1 & \cdots \\
\vdots & \vdots & \vdots & \vdots & \vdots & \ddots
\end{vmatrix}_m ,$$

where $\binom{i}{k}$ are binomial coefficients.

3.3.4 Multivariate case

All of the definitions in Section 3.3.1 for the single variable can be extended to higher-dimensional cases. Let us consider an n-dimensional stochastic variable $\vec{X} = (X_1, \ldots, X_n)$ with a probability distribution $P_n(x_1, \ldots, x_n)$. This is also known as the joint probability distribution. The probability that $X_1, \ldots, X_n$ take values between $(x_1, x_1 + dx_1), \ldots, (x_n, x_n + dx_n)$ is

$$P_n(x, 1, \ldots, x_n) dx_1 \cdots x_n.$$

From the joint probability distribution we can derive different partial distributions. As mentioned in Definition 3.8, the marginal distribution for a subset $\mathcal{Y}$

of $\mathcal{X} = (X_1, \ldots, X_n)$ can be found by integrating over the complement of the intersection of $\mathcal{Y}$ and $\mathcal{X}$. Alternatively, we can find the *conditional probability* for $X_1, \ldots, X_s$ happening given that $X_{s+1}, \ldots, X_n$ happen and have fixed values. This is denoted as $P_{s|n-s}(x_1, \ldots, x_s | x_{s+1}, \ldots, x_n)$.

3.4 Stochasticity in neuron models

In this section we take a look at a few useful definitions we will need later when further approximating neuronal behaviour. To be able to model population behaviour we need to make some assumptions and simplifications regarding our system.

3.4.1 Central limit theorem

In statistics the *central limit theorem* states that when a sample size is large enough the sampling distribution of the random variable will tend to a Gaussian distribution regardless of the distribution of a variable in a population. In short this means that when the sample size N tends to infinity the probability distribution $p(x, t)$ tends to a normal distribution.

When the theorem states that the distribution of the variable in the population does not play a role, it refers to the distribution of the values of the variable in the population from which a random sample is drawn.

The central limit applies only to variables that are both independent and identically distributed. This is why in the case of neurons we need to be aware of the fact that only in large enough populations the spiking behaviour of the neurons becomes asynchronous. This assumption of course allows the application of the central limit theorem in the first place, as the population needs to be large enough for the distributions of the independent variables to become normal. [22]

3.4.2 Diffusion approximation

The *diffusion approximation* allows us to reduce a complicated and intractable problem to a much simpler diffusion process. Diffusion tends to be preferable since it is a Markov process with continuous sample paths, making it mathematically more tractable. This approach is closely tied to the central limit theorem, as it allows us to describe a mathematically intractable sum of random variables in terms of a normal random variable which we can choose ourselves to fit our needs.[23]

In a model of a population of neurons the diffusion approximation can be performed provided that the following conditions are met:

- the amplitudes of individual synaptic currents must be small compared to the threshold value θ,

- they must have time constants much shorter than the time constant $\tau$of the system, so that they can be effectively neglected, and
- the activation of the synapses in the model must follow an independent Poisson process.

If these conditions hold we can assume that the input current consists of both a constant current $I(t)$ and a white noise term with a variance density σ^2. [13]

3.4.3 Useful distributions

Definition 3.24. [14] A *Bernoulli distribution* is a discrete distribution such that the random variable X of a probability distribution function $P(X)$ takes on one of two values; 1 (success) or 0 (failure). The probabilities of success and failure are given by $P(X = 1) = p$ and $P(X = 0) = 1 - p$, respectively. The parameter p takes values between zero and one. The distribution is given by

$$\begin{aligned} f(0) &= 1 - p, \\ f(1) &= p, \\ \mu &= p, \text{ and} \\ \sigma^2 &= p(1 - p). \end{aligned}$$

Definition 3.25. [14] A Poisson process is a continuous version of the Bernoulli process. The probabilities of events at any given time are independent of one another. In a Poisson process events happen at a rate λ that is the same for any unit time interval. The amount of events in a given time interval t will have a Poisson distribution $\mathcal{P}(\lambda t)$. The distribution is given by

$$\begin{aligned} f(x) &= \frac{1}{x!}(\lambda t)^x e^{-\lambda t}, \\ \mu &= \lambda t, \text{ and} \\ \sigma^2 &= \lambda t. \end{aligned}$$

3.5 Cable equation

We can think of a dendrite as a kind of cable connecting the soma of a neuron with another neuron. This cable can be thought to consist of multiple identical cylindrical segments with length dx. This is depicted in a circuit representation in Figure 3.1. The voltage $V(t, x)$ at position x is related with transversal and longitudinal currents. Each current causes a drop in the voltage across the transversal and the longitudinal resistor, respectively, abiding by Ohm's law. For example the longitudinal voltage drop is determined by

$$V(t, x + dx) - V(t, x) = R_L I(t, x)dx, \tag{3.16}$$

where $I(t, x)$ is the longitudinal current at time t. The transversal current is the sum of the capacitive current and the ion specific currents

$$C\frac{\partial V(t,x)}{\partial t} + \sum_i I_i(t,x), \tag{3.17}$$

where i runs through all types of ion channels. From this expression we can derive the following based on the conservation of current at each node

$$I(t, x+dx) - I(t,x) = C\left[\frac{\partial V(t,x)}{\partial t} + \sum_i I_i(t,x) - I_{ext}(t,x)\right]dx, \tag{3.18}$$

where $I_{ext}(t, x)$ is the external currents.

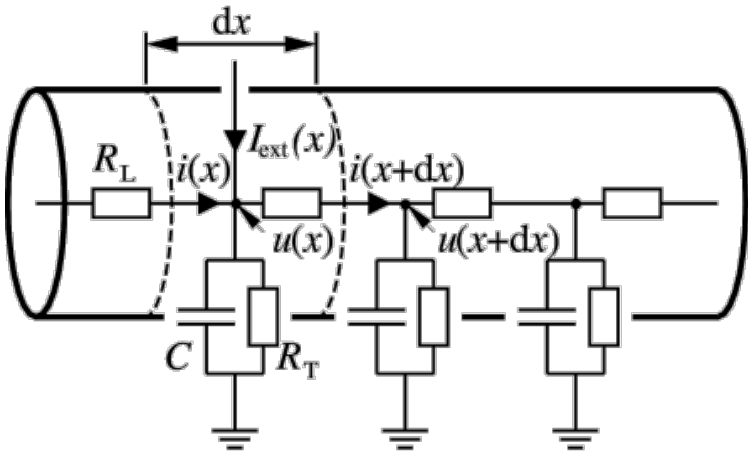

Figure 3.1: A circuit diagram depicting a dendrite in terms of the cable equation. Image from [8]. Here the membrane potential is denoted by $u(x)$.

The amount of transversal current is dependent on the length of the segment dx as the longer dx is, the more current can pass through. The longer the segment, the greater the longitudinal resistance as well as the capacitance. Using these two facts, we can take Equations (3.16) and (3.18), divide by dx and take the limit $dx \to 0$ to derive

$$\frac{\partial V(t,x)}{\partial x} = R_L I(t,x), \text{ and} \tag{3.19}$$

$$\frac{\partial I(t,x)}{\partial x} = C\frac{\partial V(t,x)}{\partial t} + \sum_i I_i(t,x) - I_{ext}(t,x). \tag{3.20}$$

When we differentiate Equation (3.19) with respect to x and substitute it into Equation (3.20) we get

$$\frac{\partial^2 V(t,x)}{\partial x^2} = CR_L\frac{\partial V(t,x)}{\partial t} + R_L\sum_i I_i(t,x) - R_L I_{ext}(t,x). \tag{3.21}$$

This is the general form of the *cable equation.*

4 The Fokker-Planck equation

The Fokker-Planck equation was originally derived for a system of particles suspended in fluid. It describes the time evolution of the probability distribution of the position of those particles as long as their movements follow a stochastic differential equation. The particles are assumed to be travelling along a continuous trajectory that is not differentiable with respect to time. The neurons in a network can be seen to behave similarly as they traverse the state space spanned by the different variables of a given model, usually the membrane potential and the conductance or input current. In the simplest form the Fokker-Planck equation has just one spatial variable x, drift $B(x,t)$, and diffusion $A(x,t)$ and it is defined by the temporal and spatial derivatives of the probability distribution $p(x,t)$

$$\frac{\partial}{\partial t}p(x,t) = -\frac{\partial}{\partial x}(B(x,t)p(x,t)) + \frac{1}{2}\frac{\partial^2}{\partial x^2}(A(x,t)p(x,t)). \tag{4.1}$$

In this section we show how the Fokker-Planck equation can be derived using the *master equation*. We shall see that the Fokker-Planck is a special case of the continuous master equation and that it gives us a recurrence relation for Markov chains in continuous time. In other words it is a differential equation describing the time evolution of the probabilities of Markov processes for systems with jump moments in continuous time. The jump moments will describe the movement of the neurons from one state to another.

At its simplest the master equation takes the form

$$\frac{dP(x,t)}{dt} = -\omega(x|x_0)P(x,t) + \omega(x_0|x)P(x,t|x_0,t_0), \tag{4.2}$$

where $\omega(x_i|x_j)$ describes the constant rate of a particle jumping to state x_i given its current state x_j and $P(x,t)$ the probability of the particle occupying state x at time t. $P(x,t|x_0,t_0)$ gives us the probability of a particle being in the state x at time t given that it was in state x_0 at time t_0. Equation (4.2) clearly describes the change in probability of a stochastic particle capable of jumping between two states being in one of those states with respect to time. The connection between Equations (4.2) and (4.1) will become clear in the following sections. We will next show how the master equation is easily generalised into the following integro-differential equation form

$$\frac{\partial p(x;t)}{\partial t} = \int [\omega(y|x)p(y;t) - \omega(x|y)p(x;t)]dy. \tag{4.3}$$

The derivation of the master equation closely follows that found in [21].

4.1 Deriving the master equation

To find the expression for the master equation we need to understand the basics of Markov processes.

4.1.1 Markov processes

For a stochastic process $Y(t)$, the conditional probability $P(y_2, t_2|y_1, t_1)$, is the probability with which $Y(t_2) = y_2$ given that $Y(t_1) = y_1$. One can now express the probability that both $Y(t_1) = y_1$ and $Y(t_2) = y_2$ happen, in that order, as

$$P(y_1, t_1; y_2, t_2) = P(y_1, t_1)P(y_2, t_2|y_1, t_1). \tag{4.4}$$

To construct the probability $P(y_1, t_1; \ldots; y_n, t_n)$, one needs to find the higher-order transition probabilities.

Definition 4.1. A stochastic process $Y(t)$ is called a *Markov chain*, or a *Markov process*, if for any set of n successive time points $t_1 < t_2 < \cdots < t_n$, one has

$$P(y_n, t_n|y_1, t_1; \ldots; y_{n-1}, t_{n-1}) = P(y_n, t_n|y_{n-1}, t_{n-1}) = P_{y_{n-1}y_n}. \tag{4.5}$$

This is to say that the probability distribution for y_n at t_n is not affected by any of the probabilities at earlier times which means that a Markov chain is fully determined by the distributions $P(y, t)$ and $P(y', t'|y, t)$.

For times $t_1 < t_2 < t_3$ we have the following;

$$\begin{aligned} P(y_1, t_1; y_2, t_2; y_3, t_3) &= P(y_1, t_1; y_2, t_2)P(y_3, t_3|y_1, t_1; y_2, t_2) \\ &= P(y_1, t_1; y_2, t_2)P(y_3, t_3|y_2, t_2) \\ &= P(y_1, t_1)P(y_2, t_2|y_1, t_1)P(y_3, t_3|y_2, t_2). \end{aligned} \tag{4.6}$$

4.1.2 Chapman-Kolmogorov equation

Proposition 4.1 (Chapman-Kolmogorov)**.** *[25] Let $n \geq 0, m \geq 0$, and let $Y(t)$ be a Markov process where $Y(t_0) = i$, $Y(t_{n+m}) = j$. Then*

$$P_{ij}^{n+m} = \sum_{k \in S} P_{ik}^n P_{kj}^m.$$

Here $P_{ik}^n = P(k, t_n|i, t_0)$ is the probability that the state at the time t_n is k, given that $Y(t_0) = i$, and S is the set of possible states.

Proof. Using the Markov property we can see that
$P(j, t_{n+m}|k, t_n; i, t_0) = P(j, t_{n+m}|k, t_n) = P(j, t_m|k, t_0) = P_{kj}^m$
and thus

$$\begin{aligned} P_{ij}^{n+m} &= P(j, t_{n+m}|i, t_0) \\ &= \sum_{k\in S} P(j, t_{n+m}; k, t_n|i, t_0) \\ &= \sum_{k\in S} \frac{P(j, t_{n+m}; k, t_n; i, t_0)}{P(i, t_0)} \\ &= \sum_{k\in S} \frac{P(j, t_{n+m}|k, t_n; i, t_0)P(k, t_n; i, t_0)}{P(i, t_0)} \\ &= \sum_{k\in S} \frac{P(k, t_n; i, t_0)P_{kj}^m}{P(i, t_0)} \\ &= \sum_{k\in S} P_{ik}^n P_{kj}^m, \end{aligned}$$

assuming that $P(i, t_0) \neq 0$. □

Integrating Equation (4.6) over y_2, we obtain

$$P(y_1, t_1; y_3, t_3) = P(y_1, t_1) \int P(y_2, t_2|y_1, t_1)P(y_2, t_2|y_1, t_1)dy_2, \tag{4.7}$$

where we write the left-hand side using the consistency of the hierarchy of distribution functions which gives us $\int P(y_1, t_1; \ldots; y_n, t_n)dy_n = P(y_1, t_1; \ldots; y_{n-1}, t_{n-1})$. Now if we divide both sides by $P(y_1, t_1)$ and use Equation (4.4), we get

$$P(y_3, t_3|y_1, t_1) = \int P(y_3, t_3|y_2, t_2)P(y_2, t_2|y_1, t_1)dy_2, \tag{4.8}$$

which is called the *Chapman-Kolmogorov equation*. Note that for this to hold t_2 must lie between t_1 and t_3. Using Equation (4.4) we can rewrite

$$P(y_2, t_2) \;=\; \int P(y_2, t_2|y_1, t_1)P(y_1, t_1)dy_2$$

in the form of

$$P(y_2, t_2) = \int P(y_1, t_1; y_2, t_2)dy_2. \tag{4.9}$$

4.1.3 The Master Equation

A master equation is a differential equation that describes the time evolution of the probabilities of a Markovian process. This is to say that we assume that when the system jumps from one state to another, the jump is not dependent on the previous states but only the current state. [21] Inspecting Equation (4.8) for equal time arguments $t_1 = t_2 = t$, we find that

$$P(y_3,t_3|y_1,t) = \int P(y_3,t_3|y_2,t)P(y_2,t|y_1,t)dy_2$$
$$\Rightarrow P(y_2,t|y_1,t) = \delta(y_2-y_1),$$

where $\delta(y_2-y_1)$ is the zeroth-order term in the behaviour of $P(y',t'|y,t)$ in a very short time interval τ. Now we can express the short-time transition probability as

$$P(y_2,t+\tau|y_1,t) = \delta(y_2-y_1)[1-a^{(0)}(y_1,t)\tau] + W_t(y_2|y_1)\tau + \mathcal{O}[\tau^2], \tag{4.10}$$

where $W_t(y_2|y_1)$ is the transition probability from y_1 to y_2 at time t per unit time, and $1-a^{(0)}(y_1,t)\tau$ is the probability that no transition takes place during the time τ. If we now set the integral of $P(y_2,t_2|y_1,t_1)$ with respect to y_2 on the interval τ to 1 we get

$$1 = \int P(y_2,t+\tau|y_1,t)dy_2 \simeq 1 - a^{(0)}(y_1,t)\tau + \int W_t(y_2|y_1)\tau dy_2.$$

With this we arrive at

$$a^{(0)}(y_1,t) = \int W_t(y_2|y_1)dy_2. \tag{4.11}$$

Clearly $a^{(0)}(y_1,t)\tau$ is the total probability of escape from y_1 in the interval $(t,t+\tau)$. Now we can use the Chapman-Kolmogorov equation to derive the differential equation for the transition probability. By inserting the above short-time expression of the transition probability into Equation (4.8) we get

$$\begin{aligned} P(y_3,t_2+\tau|y_1,t_1) &= \int P(y_3,t_2+\tau|y_2,t_2)P(y_2,t_2|y_1,t_1)dy_2 \\ &\simeq [1-a^{(0)}(y_3,t_2)\tau]P(y_3,t_2|y_1,t_1) \\ &\quad + \tau\int W_{t_2}(y_3|y_2)P(y_2,t_2|y_1,t_1)dy_2. \end{aligned}$$

Next we use Equation (4.11) to rewrite $a^{(0)}(y_3,t_2)$ in terms of $W_{t_2}(y_2|y_3)$ to arrive at

$$\begin{aligned} &\frac{1}{\tau}\Big[P(y_3,t_2+\tau|y_1,t_1) - P(y_3,t_2|y_1,t_1)\Big] \\ &\simeq \int \Big[W_{t_2}(y_3|y_2)P(y_2,t_2|y_1,t_1) \\ &- W_{t_2}(y_2|y_3)P(y_3,t_2|y_1,t_1)\Big]dy_2, \end{aligned}$$

which then in the limit $\tau \to 0$ yields the *master equation*. After some changes in notation we get

$$\frac{\partial}{\partial t}P(y,t|y_0,t_0) = \int \Big[W_t(y|y')P(y',t|y_0,t_0) - W_t(y'|y)P(y,t|y_0,t_0)\Big]dy', \tag{4.12}$$

which is an integro-differential equation. The master equation can be extended to the case of a multi-component Markov chain $Y_i(t), i = 1, 2, \ldots, N$ by replacing y with a vector $y = (y_1, \ldots, y_N)$ in the Chapman-Kolmogorov Equation (4.8), to yield the multivariate counterpart of the master Equation [20]

$$\frac{\partial P(y,t)}{\partial t} = \int [W(y|y')P(y',t) - W(y'|y)P(y,t)]dy'. \tag{4.13}$$

4.2 The Fokker-Planck equation

In this section we will derive the Fokker-Planck equation using the master equation. Here it is important to note that the reason we don't want to use the master equation to represent our system of neurons it that the master equation is an integro-differential equation and can thus be very complicated to solve. Using the Kramers-Moyal expansion, as shown in the next section, allows us to simplify the master equation to get a continuous partial differential equation.

4.2.1 Kramers-Moyal expansion

The Kramers-Moyal expansion transforms the integro-differential master equation to a partial differential equation through a Taylor series expansion. This section closely follows the derivation in [20]. Let us use a change of variables to express the transition probability W as

$$W(y|y') = W(y'; r), \tag{4.14}$$

where $W(\cdot;\cdot)$ is a function of $r = y - y'$, the size of a jump from state y' to state y. The master Equation (4.12) can now be written as

$$\frac{\partial P(y,t)}{\partial t} = \int W(y-r;r)P(y-r,t)dr - P(y,t)\int W(y;-r)dr. \tag{4.15}$$

If we assume the changes on y to occur in small jumps and $P(y,t)$ to vary slowly with y, we can then use a Taylor expansion to express the shift between the states y and $y - r$ in the first integral of Equation (4.15)

$$\begin{aligned}\frac{\partial P(y,t)}{\partial t} &= \int W(y;r)P(y,t)dr + \sum_{m=1}^{\infty}\frac{(-1)^m}{m!}\int r^m \frac{\partial^m}{\partial y^m}[W(y;r)P(y,t)]dr \\ &\quad - P(y,t)\int W(y;-r)dr \\ &= \sum_{m=1}^{\infty}\frac{(-1)^m}{m!}\frac{\partial^m}{\partial y^m}\Big\{\Big[\int r^m W(y;r)dr\Big]P(y,t)\Big\},\end{aligned}$$

where the first and third terms on the right-hand side cancelled each other due to the symmetry of $W(\cdot;\cdot)$. When we now introduce the jump moments

$$a^{(m)}(y,t) = \int r^m W(y;r)dr, \tag{4.16}$$

we arrive at the *Kramers-Moyal expansion* of the master equation

$$\frac{\partial P(y,t)}{\partial t} = \sum_{m=1}^{\infty}\frac{(-1)^m}{m!}\frac{\partial^m}{\partial y^m}[a^{(m)}(y,t)P(y,t)]. \tag{4.17}$$

It is now possible to remove larger terms by declaring $a^{(m)}(y,t)$ to be negligible when m is greater than 2, for instance. This is now the diffusion approximation which, according to the central limit theorem, is exact in the limit of infinitely large networks [13]. We discussed this method earlier in Section 3.4.2. In this case we are left with

$$\frac{\partial P(y,t)}{\partial t} = -\frac{\partial}{\partial y}[a^{(1)}(y,t)P(y,t)] + \frac{1}{2}\frac{\partial^2}{\partial y^2}[a^{(2)}(y,t)P(y,t)], \tag{4.18}$$

which is now the *Fokker-Planck equation.* The first term is called the *drift term* and the second the *diffusion term*, while $a^{(1)}(y,t)$ and $a^{(2)}(y,t)$ are the *drift and diffusion coefficients.*

The Fokker-Planck equation, as a special case of the Kramers-Moyal expansion of the master equation, involves the transition probability $P(y,t|y_0,t_0)$ of the Markov stochastic process, not its one-time probability distribution $P(y,t)$. In order to calculate the jump moments $a^{(m)}(y,t)$ we use the relation between the transition probability per unit time $W(y'|y)$ and that for short-time transition, seen in Equation (4.10).

From Equation (4.14) we see that $W(y';r) = W(y|y')$, where $r = y - y'$. Using this we find that

$$\begin{aligned}&W(y';r) = W(y+r;r) = W(y|y') = W(y'-r|y+r) \\ &\text{and so} \\ &W(y;r) = W(y'-r;r) = W(y'|y).\end{aligned} \tag{4.19}$$

Inserting this into Equation (4.16) we can write the jump moment in the following way

$$a^{(m)}(y,t) = \int (y'-y)^m W(y'|y)dy'. \tag{4.20}$$

Using the quantity

$$\mathcal{A}^{(m)}(y;\tau,t) = \int (y'-y)^m P(y',t+\tau|y,t)dy', \qquad (m \geq 1),$$

we can now calculate the jump moments. This is the average $[Y(t+\tau)-Y(t)]^m$ with initial value $Y(t) = y$. Now using Equation (4.10) we get

$$\begin{aligned}
\mathcal{A}^{(m)}(y;\tau,t) &= \int (y'-y)^m \{\delta(y'-y)[1-a^{(0)}(y,t)\tau] + W(y'|y)\tau + \mathcal{O}(\tau^2)\}dy' \\
&= \tau \int (y'-y)^m W(y'|y)dy' + \mathcal{O}(\tau^2) \\
&= a^{(m)}(y,t)\tau + \mathcal{O}(\tau^2), \qquad (m \geq 1),
\end{aligned}$$

where δ is the Dirac delta distribution which allows the integral involving the first term in the short-time transition probability to vanish. The Dirac delta distribution is defined as a distribution with three main properties:

- if $y \neq y'$, then $\delta(y'-y) = 0$,
- $\int_{y-\varepsilon}^{y+\varepsilon} \delta(y'-y)dy' = 1, \varepsilon \geq 0$, and
- $\int_{y-\varepsilon}^{y+\varepsilon} f(y')\delta(y'-y)dy' = f(y)$,when $\varepsilon \geq 0$.

Assuming $A^{(m)}(y;0,t) = 0$, the jump moments can be calculated from the derivatives of the conditional averages in the following way

$$a^{(m)}(y,t) = \frac{\partial}{\partial \tau}\mathcal{A}^{(m)}(y;\tau,t)\bigg|_{\tau=0}.$$

If we now write

$$\mathcal{A}^{(m)}(y;\Delta t,t) = \int (y'-y)^m P(y',t+\Delta t|y,t) = \Big\langle [Y(t+\Delta t)-Y(t)]^m \Big\rangle\bigg|_{Y(t)=y},$$

we get the following expression for the jump moments

$$a^{(m)}(y,t) = \lim_{\Delta t \to 0} \frac{1}{\Delta t}\Big\langle [Y(t+\Delta t)-Y(t)]^m \Big\rangle\bigg|_{Y(t)=y}. \tag{4.21}$$

5 Mean-field models in neuroscience

In this chapter we take a look at three different population models that make use of the mean-field approximation. These models have different properties both mathematically and biologically. The main motivation behind choosing the following three models was to give the reader an idea of how different some of the approaches under the mean-field umbrella can be and how these methods can be chosen to fit a particular biological situation based on what characteristic of the network we are interested in. This also applies to the biological accuracy the model is trying to achieve. The first model we introduce is the ensemble density model which uses the Fokker-Planck formalism to approximate a network of neurons with asynchronous behaviour. In this case the network is reduced to a rate model of the spiking of individual neurons which of course is a gross simplification, but an apt one when we are interested in the network spiking behaviour only. The second model uses a computational geometry based method to find a mean-field approximation for a one or two dimensional neuronal model, which allows us to consider various types of stochastic processes, unlike the ensemble density method. This allows us to study not only asynchronous Gaussian behaviour but also spiking in more inter-connected and synchronised networks. Finally the third model is slightly more biologically relevant, as it takes into account the fact that signal propagation in neurons is not instantaneous in vivo. This is done by incorporating the cable equation into the system in order to approximate signal propagation along the dendritic tree of a neuron.

So what exactly defines the point of interest of a certain network model? As the mechanisms driving neuronal function are in fact very complex, suitable simplifications and approximations are often essential. As previously discussed in Chapter 2, information transfer between neurons is based on the changes in the resting membrane potential of the cell, that is, the electrical potential of the intracellular space in comparison with the outside of the cell. A message received from another neuron causes the resting membrane potential to change, resulting in a postsynaptic potential in the receiving cell. This change in potential is due to the flow of charged particles between the neural cell and its surrounding extracellular space.[13]

These ions flow from the cell to the extracellular space and vice versa through specialised ion channels on the cell surface. When the postsynaptic potential reaches a critical threshold, the neuron fires an action potential, or spike which in turn acts as an input for the next neuron, causing the message to be relayed further. When we are interested in the network behaviour of a population of neurons the detailed ion flows are irrelevant to the bigger picture. Instead, we focus on the population and the depolarisation caused by the influx of positive ions leads to the neuron firing. The firing of these action potentials can be described in terms of the spike times, and the resulting spiking behaviour can

be used to represent the cell as a part of a network. The mean-field approach can be used to reduce such large populations of spiking neurons to a distribution function describing the time evolution of the distribution of neuronal states. Again the state tells us whether the neuron is spiking or not. In simpler terms, the resulting distribution function gives us the probability of different neurons firing at a given time. As a side note, because mean-field models describe population level activity they are especially suited to biophysically recorded data such as EEG, MEG, and fMRI [13].

5.1 Ensemble density models

The main motivation for using ensemble density models of neurons is their ability to describe the dynamics of very large, or theoretically infinite, populations. As the higher level functions of the brain are thought to arise from the population behaviour of networks of neurons, it is only sensible to try and approximate their behaviour on the mesoscopic scale. When we make the assumption that population level activity is asynchronous, we can use the steps covered in Chapter 4 to derive a probability distribution function for the spiking behaviour of the theoretically infinite population of neurons we are interested in. The model that we consider in this section can be found in [13].

First we will look at the single cell LIF model originally introduced in Section 2.2.3. Each attribute of a single neuron induces a dimension in the phase space; in this case the LIF neurons have a three-dimensional state space where each point corresponds to some $\nu(t) = (V(t), I(t), T(t))^T \in \mathbb{R}^3$, where $V(t)$ is the postsynaptic membrane depolarisation, $I(t)$ the capacitive current, and $T(t) > 0$ the time elapsed since the last spike. When the population size approaches infinity the points in the phase space have the density $p(\nu(t), t)$. The dynamics of this scalar function conform to the Fokker-Planck equation, the temporal evolution of which is rather simple to approximate using the mean-field approach. A visualisation of the marginal probability density of one such mean-field model is shown in 5.1.

To derive the model for a large network of neurons we have to first start at the single neuron level. Most often these ensemble density models use simple, point-like, one-compartment models, and here we will be using the leaky-integrate-and-fire (LIF) model, in which each neuron i can be represented by just the depolarisation $V_i(t)$ of their neural membrane, as mentioned in Section 2.2.3. We create a network of these neurons by giving the population a size N and assuming that each neuron i is connected to another with a synapse with connection J_{ij}, where J is a matrix for the synaptic strengths between the interconnected neurons. According to the central limit theorem the spiking behaviour approaches a Gaussian distribution, allowing us to describe the population using a probability distribution function. Again, as in Chapter 4 we derive the Kramers-Moyal expansion of the probability function by first taking the Taylor expansion and then the limit when $dt \to 0$, giving us the probabil-

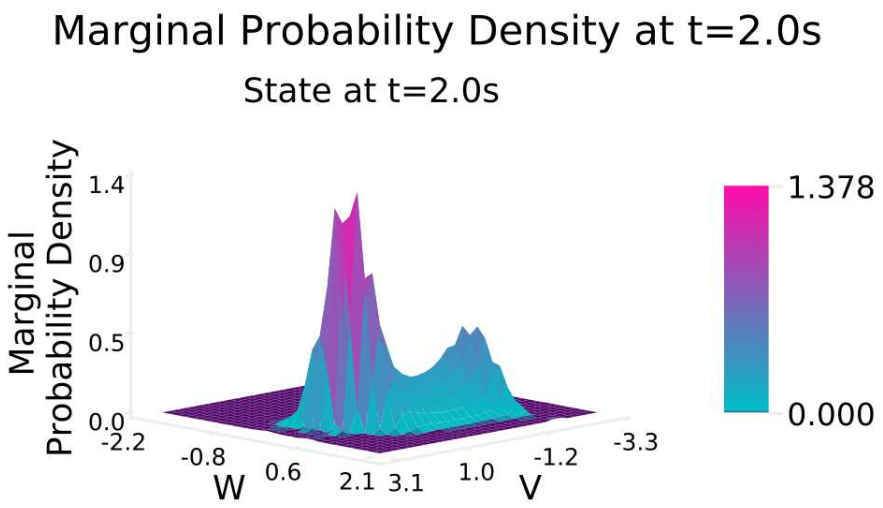

Figure 5.1: The marginal probability density of a simulated mean-field of FitzHugh-Nagumo neurons. Figure from [24].

ity density of the population over time. We use the diffusion approximation to replace the individual synaptic strengths between the connected neurons by their averages, which gives us the Fokker-Planck representation of our original population of neurons. We will go over the steps of deriving this representation in the next section.

5.1.1 Deriving the Fokker-Planck representation

The properties of the neuron can be described by a simple RC circuit, where the membrane acts as a capacitor C in parallel with a resistor R that is driven by the synaptic current. In order for the neuron to fire the voltage across its membrane (capacitor) has to reach a threshold θ, generating an action potential δ after which the voltage is then reset. When the membrane potential remains below the threshold value θ the voltage evolves according to a simple RC circuit with a time constant $\tau = RC$ given by

$$\tau \frac{dV_i(t)}{dt} = -[V_i(t) - V_L] + RI_i(t), \tag{5.1}$$

where V_L stands for the resting potential and $I_i(t)$ denotes of the total synaptic current, assumed to be comprised of all of the action potentials produced by the presynaptic neurons flowing into the neuron i. Let us assume we have N neurons connected to neuron i with J_{ij} denoting the efficacy of the synapse between neurons i and j, then we have

$$RI_i(t) = \tau \sum_{j=1}^{N} J_{ij} \sum_k \delta(t - t_j^{(k)}), \tag{5.2}$$

where $t_j^{(k)}$ denotes the time elapsed from the time the kth spike was fired from the jth presynaptic neuron until the message reaches the cell i. If we assume that at time $t = 0$ the neuron i has the resting potential V_L, and plug Equation (5.2) into Equation (5.1) and integrate it, we are left with

$$\begin{aligned} V_i(t) =& V_L + \sum_{j=1}^{N} J_{ij} \int_0^t e^{-s/\tau} \sum_k \delta(t - s - t_j^{(k)}) ds, \\ =& V_L + \sum_{j=1}^{N} J_{ij} e^{-(t-t_j^{(k)})/\tau} \sum_k H(t - t_j^{(k)}), \end{aligned}$$

In the above expression H denotes the Heaviside step function, where $H(t) = 1$ for every $t > 0$, and otherwise $H(t) = 0$. This acts as a filter for the incoming pulse δ from the presynaptic cell producing either an excitatory or inhibitory postsynaptic potential (EPSP or IPSP, respectively). The spiking threshold reset makes the LIF model highly nonlinear which calls for an approach capable of dealing with this kind of behaviour such as the Fokker-Planck equation. The way that the Fokker-Planck equation describes the evolution of the states over the phase space is well suited for representing the population dynamics of neural cells. Here we derive a mean-field model for a network of spiking neurons starting with dividing the neurons into populations based on their behaviour. Statistically similar neurons can be grouped together and each population can then be described by a probability density function of the neuronal states over the population. Because we can assume that any given neuron with state $V(t)$ at a given time t has arrived at that state through a set of markovian steps, as mentioned in Definition 4.1, the neurons sharing that state are virtually indistinguishable and the evolution of the population dynamics can then be described by a probability density function

$$p(v, t)dv = P(V(t) \in [v, v + dv]), \tag{5.3}$$

which expresses the fraction of the population that at time t has a membrane potential $V(t)$ in the interval $[v, v + dv]$. The time evolution of this population density is given by the Chapman-Kolmogorov equation (3.4) which we can now write in the following way

$$p(v, t + dt) = \int p(v - \varepsilon, t)\rho(\varepsilon|v - \varepsilon)d\varepsilon, \tag{5.4}$$

where $V(t) = v, V(t + dt) = v + \varepsilon$, and $\rho(\varepsilon|v) = P(v + \varepsilon|v)$ describes the conditional probability which in the interval dt generates the change ε. Performing a Taylor Expansion in $p(v', t)\rho(\varepsilon|v')$ at $v' = v$, substituting this to Equation (5.4) and replacing the time derivative in v' by the equivalent time derivative

in v, we have

$$\begin{aligned} p(v,t+dt) &= p(v,t)\int \rho(\varepsilon|v)d\varepsilon - \frac{\partial}{\partial v}\Big[p(v,t)\Big(\int \varepsilon\rho(\varepsilon|v)d\varepsilon\Big)\Big] \\ &\quad + \frac{1}{2}\frac{\partial^2}{\partial v^2}\Big[p(v,t)\Big(\int \varepsilon^2\rho(\varepsilon|v)d\varepsilon\Big)\Big] + \ldots, \\ &= \sum_{k=0}^{\infty}\frac{(-1)^k}{k!}\frac{\partial^k}{\partial v^k}[p(v,t)\langle\varepsilon^k\rangle_v], \end{aligned}$$

where $\langle\ldots\rangle_v$ denotes the average at a given v with respect to $\rho(\varepsilon|v)$. Now, taking the limit $dt \to 0$ again leaves us with the Kramers-Moyal expansion

$$\begin{aligned} \lim_{dt\to 0}\frac{\partial p(v,t+dt)}{\partial t} &= \lim_{dt\to 0}\sum_{k=0}^{\infty}\frac{(-1)^k}{k!}\frac{\partial^k}{\partial v^k}\Big[p(v,t)\langle\varepsilon^k\rangle_v\Big] \\ \frac{\partial p(V(t),t)}{\partial t} &= \sum_{k=1}^{\infty}\frac{(-1)^k}{k!}\frac{\partial^k}{\partial V(t)^k}\Big[p(V(t),t)\lim_{dt\to 0}\langle[V(t+dt)-V(t)]^k\rangle_{V(t)}\Big] \\ \frac{\partial p(V(t),t)}{\partial t} &= \sum_{k=1}^{\infty}\frac{(-1)^k}{k!}\frac{\partial^k}{\partial V(t)^k}\Big[p(V(t),t)\lim_{dt\to 0}\frac{\langle dV(t)^k\rangle_{V(t)}}{dt}\Big] \\ &= \sum_{k=1}^{\infty}\frac{(-1)^k}{k!}\frac{\partial^k}{\partial v^k}\Big[p(v,t)\lim_{dt\to 0}\frac{1}{dt}\langle\varepsilon^k\rangle_v\Big], \end{aligned} \tag{5.5}$$

which represents the evolution of the probability density over time in differential form. Just as we did in Section 4.2, we can now perform the diffusion approximation and thus ignore the higher order terms by declaring them to be negligible when $k > 2$. The jump moments $\langle\varepsilon\rangle_v$ are an essential part of the Kramers-Moyal expansion of our spiking neural network, as we will soon see.

This is where the mean-field approximation comes in, as we can replace the time-averaged firing rates of individual neurons with the ensemble average. The mean population firing rate can be determined by

$$Q(t) = \lim_{dt\to 0}\frac{n(t,t+dt)}{Ndt}, \tag{5.6}$$

where $n(t,t+dt)$ is the number of spikes in each neuron during the infinitesimal interval dt. when our population size N tends to infinity the behaviour of individual neurons averages out. Here this means that we can assume that all of the synaptic strengths are the same as well as the amount of spikes each neuron emits. Because of this we can now replace the individual synaptic efficacies by the population average so that

$$\sum_{j=1}^{N} J_{ij} = \langle J\rangle_J,$$

and the amount of spikes in the population so that

$$\sum_k \delta(t - t_j^{(k)}) = NQ(t).$$

Now Equation (5.2) for individual neurons becomes

$$RI(t) = \tau \langle J \rangle_J NQ(t) \tag{5.7}$$

for the average neuron. We can now manipulate Equation (5.1) to find the average change in the membrane potential

$$\begin{aligned} \tau \frac{dV(t)}{dt} &= -[V(t) - V_L] + RI(t) \\ &= -[V(t) - V_L] + \tau \langle J \rangle_J NQ(t) \\ \implies dV(t) &= -\frac{dV(t) - V_L}{\tau} dt + \langle J \rangle_J NQ(t) dt, \end{aligned}$$

and finally we arrive at

$$dV(t) = \langle J \rangle_J NQ(t) dt - \frac{V(t) - V_L}{\tau} dt, \tag{5.8}$$

which allows us to model the average infinitesimal change in the membrane potential $dV(t)$. Here N is again the number of neurons, $\langle J \rangle_J$ is averaged synaptic weight, and $Q(t)$ is again the average firing rate of the population.

As we again used the diffusion approximation to ignore the higher-order terms of the Kramers-Moyal expansion, we only need to deal with the first and second jump moments. The first and second moments can be found using Equation (5.8) and the fact that $\varepsilon = dV(t)$.

$$a^{(1)} = \lim_{dt \to 0} \langle \varepsilon \rangle_v = \langle J \rangle_J NQ(t) - \frac{v - V_L}{\tau} = \frac{\mu(t)}{\tau} - \frac{v - V_L}{\tau}, \text{ and} \tag{5.9}$$

$$a^{(2)} = \lim_{dt \to 0} \langle \varepsilon^2 \rangle_v = \langle J^2 \rangle_J NQ(t) = \frac{\sigma^2}{\tau}, \tag{5.10}$$

The first moments are the drift and diffusion coefficients, respectively.

When we plug these into Equation (5.5) we are left with the Fokker-Planck equation, which in this case has the form

$$\frac{\partial p(v,t)}{\partial t} = \frac{1}{2\tau} \sigma^2(t) \frac{\partial^2 p(v,t)}{\partial v^2} + \frac{\partial}{\partial v} \Big[\Big(\frac{v - V_L - \mu(t)}{\tau} p(v,t) \Big) \Big]. \tag{5.11}$$

We will solve the Fokker-Plack equation for the case where the drift is linear and the diffusion constant. In this case the Fokker-Planck equation describes the stochastic Ornstein-Uhlenbeck process for the time evolution of the membrane potential $V(t)$. In this case the currents affecting the membrane potential are given by the following equation

$$RI(t) = \mu(t) + \sigma \sqrt{\tau} \omega(t), \tag{5.12}$$

where $\omega(t)$ is the white noise element. Using the central limit theorem we can interpret the above equation as a case where the sum of many Poisson processes becomes a normal random variable with mean $\mu(t)$ and variance $\sigma^2(t)$.

5.1.2 Solving the Fokker-Planck equation

Integrating the non-stationary solutions of the Fokker-Planck equation would allow for explicit simulation of the network dynamics but these simulations would be computationally demanding. However, the mean-field approach ensures that the stationary solutions of the Fokker-Planck equation, that is, the solutions where all the time derivatives are equal to 0, converge to a stationary attractor consistent with the steady-state behaviour of the original LIF system. We will now take a look at the stationary solutions for our mean-field model describing the Ornstein-Uhlenbeck process mentioned above with the mean and the variance $\mu(t) = \langle J \rangle_J NQ(t)$ and $\sigma^2(t) = \langle J^2 \rangle_J NQ(t)$, respectively. Equation (5.11) can be written as a continuity equation

$$\frac{\partial p(v,t)}{\partial t} = -\frac{\partial F(v,t)}{\partial v}, \tag{5.13}$$

where

$$F(v,t) = -\frac{v - V_L - \mu(t)}{\tau} p(v,t) - \frac{\sigma^2(t)}{2\tau} \frac{\partial p(v,t)}{\partial v} \tag{5.14}$$

is the flux of probability. We have the following boundary condition for the stationary solution

$$p(\theta, t) = 0. \tag{5.15}$$

This boundary condition describes the threshold jump in voltage, meaning that the probability of any neuron having the membrane potential of exactly θ is zero because when the threshold is reached, the probability mass moves almost instantaneously to the resting membrane potential V_r. At the threshold θ the probability current should give us the mean firing rate Q of the population, and thus

$$\frac{\partial p(\theta,t)}{\partial v} = -\frac{2Q(t)\tau}{\sigma^2(t)} \tag{5.16}$$

must hold.

Furthermore, at $v \to \theta$ the probability density vanishes fast enough to be integrable. This means that

$$\lim_{v \to -\infty} p(v,t) = 0, \tag{5.17}$$

and

$$\lim_{v \to -\infty} vp(v,t) = 0. \tag{5.18}$$

Let t_r be the refractory period of the neurons, that is, the time it takes for the cell to be able to fire after having reset its membrane potential after a spike. Now the probability mass leaving the threshold at time t has to be plugged back in at reset potential at time $t + t_r$ which then leads to the expression

$$\frac{\partial p(v,t)}{\partial t} = -\frac{\partial}{\partial v}\Bigg[F(v,t) + Q(t-t_r)H(v-V_r),\Bigg] \tag{5.19}$$

where H again denotes the Heaviside function. When we plug Equation (5.14) into the above expression we get

$$\begin{aligned} \frac{\partial p(v,t)}{\partial t} &= -\frac{\partial}{\partial v}\Bigg[-\frac{v - V_l - \mu(t)}{\tau}p(v,t) - \frac{\sigma^2(t)}{2\tau}\frac{\partial p(v,t)}{\partial v} \\ &\quad + Q(t-t_r)H(v-V_r)\Bigg] \end{aligned} \tag{5.20}$$

$$\begin{aligned} &= \frac{\partial p(v,t)}{\partial v}\left(\frac{v - V_L - \mu(t)}{\tau}\right) + \frac{\partial^2 p(v,t)}{\partial v^2}\frac{\sigma^2(t)}{2\tau} \\ &\quad - \frac{\partial}{\partial v}Q(t-t_r)H(v-V_r) \end{aligned} \tag{5.21}$$

Now using the following fractional Fourier transform with respect to the membrane potential v

$$\tilde{p}(w,t) = [\mathcal{F}_v(p(v,t))]^{(W)} = \int_{-\infty}^{\infty} p(v,t)e^{-iwv}dv, \tag{5.22}$$

we get

$$\frac{\partial \tilde{p}(w,t)}{\partial t} = -iw\left[\left(-\frac{i}{\tau}\frac{\partial}{\partial w} + \frac{-V_L - \mu(t)}{\tau}\right)(\tilde{p})(w,t)\right] - \frac{\sigma^2(t)}{2\tau}w^2\tilde{p}(w,t). \tag{5.23}$$

If we manipulate this to get

$$\frac{\partial \tilde{p}(w,t)}{\partial t} + \frac{w}{\tau}\frac{\partial}{\partial w}\tilde{p}(w,t) = -\left[\frac{iw(-V_L - \mu(t))}{\tau} + \frac{\sigma^2(t)}{2\tau}w^2\right]\tilde{p}(w,t), \tag{5.24}$$

we can use the method of characteristics. If we also plug in the boundary conditions we arrive at the solution

$$i\tilde{p}(w,t) = \frac{2Q\tau}{\sigma(t)}\exp\left(-\frac{w - V_L - \mu(t)}{\sigma^2(t)}\right)\int_{\xi_0}^{\xi_1} H\left(x - \frac{V_r - V_L - \mu(t)}{\sigma(t)}\right)e^{x^2}dx, \tag{5.25}$$

where

$$\xi_0(t) = \frac{\theta - V_L - \mu(t)}{\sigma(t)}$$

and

$$\xi_1(t) = \frac{w - V_L - \mu(t)}{\sigma(t)}.$$

This solution can be found in detail in [26].

The fraction of neurons that are silent, meaning that they are incapable of firing, can be calculated from the mean firing rate and the refractory period; $Q(t)_r$. When we account for these silent neurons and normalise the probability mass we arrive at the expression

$$\int_{-\infty}^{\theta} \tilde{p}(w,t)dw + Q(t)_r = 1, \tag{5.26}$$

where the probability of a neuron in either a state spiking or not spiking and the probability of a neuron being in the refractory period adds up to 1.

Now plugging the stationary solution to the above equation and solving for $Q(t)$ yields the Ricciardi population transfer function ϕ

$$Q(t) = \left[t_r + \tau\sqrt{\pi} \int_{\xi_2(t)}^{\xi_0(t)} e^{x^2}(1 + \mathrm{erf}(x))dx\right]^{-1} = \phi(\mu, \sigma), \tag{5.27}$$

where

$$\xi_2(t) = \frac{V_r - V_L - \mu(t)}{\sigma(t)}$$

and

$$\mathrm{erf}(x) = \frac{2}{\sqrt{\pi}} \int_0^x e^{-y^2} dy$$

is the error function that arises from integrating the normal distribution. The stationary dynamics of different cell populations are given by the transfer function of that population. It can easily be generalised for the different neuronal populations that are grouped based on their statistical similarities, e.g. inhibitory and excitatory neuron populations. The neurons in each group will share an identical independent firing rate as well as the same Gaussian distribution. The population transfer function gives us the average population rate and its dependence on the average current of each population. When we solve a set of self-consistency equations

$$Q_i(t) = \phi(\mu_i(t), \sigma_i(t)), \tag{5.28}$$

for all i, we need to integrate the following differential equation

$$\tau_k \frac{dQ_k(t)}{dt} = -Q_k(t) + \phi(\mu_k(t), \sigma_k(t)). \tag{5.29}$$

This leaves us with a set of stationary self-producing rates $Q_i(t)$. Now it is possible for us to choose our parameters afterwards to be able to match the type of behaviour we are looking for. We can use the acquired parameters to simulate the full LIF system in all of the non-stationary states as well as the stationary ones. This allows the derivation of the original dynamical behaviour of the underlying LIF model, as the dynamics of the mean-field system converge towards a stationary attractor which is consistent with the underlying LIF system. Thus we have now found the transfer function ϕ which correctly mimics the original leaky integrate-and-fire model, and corresponds with the assumptions we made about the system in the beginning.[13]

5.2 Computational geometry model

The method proposed by de Kamps et al. in [27] aims to combat the limitations of the Fokker-Planck formalism. Using this method one does not perform the diffusion approximation nor does one reduce the state space into a one dimensional (1D) space. Using this approach the neural populations can be simulated both in 1D or by using two dimensional (2D) spiking neuron models that offer a richer repertoire of dynamical behaviour compared to those in 1D. In this section we will be looking at a 2D model based on the Izhikevich model described in Section 2.2.4. This is to present the reader with the full benefits of this approach.

As this method does not rely on the diffusion approximation, it allows us to consider a variety of differing stochastic processes, as long as the state space is subject to a Poisson spike process. This means that the timing of the action potential firing has to follow a Poisson distribution. Where as the Fokker-Planck approach fails when the system exhibits synchronised network behaviour, the computational geometry method is able to accurately model populations that have partial synchrony, meaning that we don't need to make assumptions about the asynchronous behaviour of the network.

In the following sections we will first derive the mean-field representation of the network. This is done assuming the spike trains to be Markovian which allows us to use the Chapman-Kolmogorov equation. Unlike in the ensemble density model we will not perform the Kramers-Moyal expansion but instead transform the PDE system into a system of ODEs by introducing a change of coordinates. We will then provide the reader with a short example of the steps needed to solve the system.

5.2.1 Deriving the system

Here, for simplicity, we will use x to denote the first component of the vector v which is the membrane potential, and y to denote the second coordinate which – depending on the underlying single cell model – can be either the conductance or the input current. In the model we use here y stands for the conductance

of the cell membrane. As the point neuron network we consider here has a two dimensional phase space, the model is best described by a vector field F defined on an open subset $M \subseteq \mathbb{R}^2$ giving us the following equation for the movement of a single neuron in the phase space

$$\tau \frac{dv}{dt} = F(v), \tag{5.30}$$

where τ is again the membrane time constant of the neuron defined earlier in Equation (5.1), and $v \in \mathbb{R}^2$ is the state of the system.

In the two dimensional case we will also have a threshold value θ for the membrane potential $x \in \mathcal{V}$, where $\mathcal{V}$ is the domain of the membrane potentials. When $x = \theta$ it overlaps with a part of ∂M. We call this area of overlap the threshold. Again, when the neuron state v reaches the threshold, the membrane potential x is reset to the reset potential V_r, after a refractive time interval t_r. The second coordinate usually stays unchanged unless the refractory period is considered to have an effect on the variable. This depends on the model on which this method will be used, as what y stands for varies. In the Izhikevich model y represents the conductance of the neuronal membrane. The reset value of y is normally the resulting value of $y(t + t_r)$, where t is the time at the moment the neuron last spiked.

Here we are nevertheless interested not in single neurons but populations of them. We assume these populations to be homogeneous, that is, they consist of statistically similar neurons, so we can represent a sufficiently large population again by a density $p(v, t)$ over its state space.

The spike trains are again assumed to be Markovian in nature allowing us to use the Chapman-Kolmogorov equation (4.8) to represent the evolution of the density in time. In this case the equation takes the following form

$$\frac{\partial p(t)}{\partial t} + \frac{\partial}{\partial v} \times \Big(\frac{F(v)p(t)}{\tau}\Big) = \int_M \Big[W(v|v')\rho(v') - W(v'|v)\rho(v)\Big]dv', \tag{5.31}$$

where $\rho(v)dv$ represents the fraction of neurons with a state in dv, and Equation (5.30) gives us F and τ. The operator $\times$ is defined as

$$\times \begin{pmatrix} v_1 \\ v_2 \end{pmatrix} \equiv \begin{pmatrix} -v_2 \\ v_1 \end{pmatrix},$$

The responses of the state space of the neurons to input spikes will be instantaneous. For example, if we consider a delta spike δ it will cause the membrane potential to rise by an amount h, which here denotes the synaptic efficacy. So the membrane potential will rise from x to $x + h$, where h can be drawn from a probability distribution $w(h)$. Depending on whether the model is based on the input current or conductance, the jump h will affect the membrane potential or the conductivity, respectively. The right-hand side of the Chapman-Kolmogorov equation above states that when affected by the jump the fraction

of neurons that moves away from one state reappears in another, as the size of the population is naturally constant. As an example we can consider a spike train generated by a Poisson process

$$W(x'|x) = \nu\delta(x' - x - h) + (1 - x)\delta(x - x'), \tag{5.32}$$

where δ is a delta spike, ν is the rate of the Poisson process, and h again the synaptic efficacy. Here we consider h to be constant, in the name of simplicity. With these assumption we can take Equation (5.31) and reduce it to

$$\frac{\partial p(t)}{\partial t} + \frac{\partial}{\partial v} \times \Big(\frac{F(v)p(t)}{\tau}\Big) = \nu(\rho(v-h, v_1, \ldots, v_{n-1}) - \rho(v, v_1, \ldots, v_{n-1})), \tag{5.33}$$

where $v_i, i \in \{1, \ldots, n-1\}$, is the i^{th} component of the vector v.

In the ensemble density model we would use the Kramers-Moyal expansion and the diffusion approximation to derive the Fokker-Planck equation (4.18). Here we will instead use the method of characteristics and introduce a new coordinate system to transform the system in our model from a partial differential equation into an ordinary differential equation. If we take a point s on a line l in the state space, such that $s = v_0$ at time $t = 0$, then the system of ordinary differential equations in Equation (5.30) describes the evolution of the point v_0 on an integral curve of the vector field $F(v)$. The curve may be found through integration. Writing this curve as $\omega(t, v_0)$ lets us introduce the following change of coordinates

$$\begin{aligned} x \to x' &= \omega(t, v_0) \\ t \to t' &= t. \end{aligned}$$

Using this new coordinate system we can manipulate Equation (5.31) into the form of a Poisson master equation

$$\frac{dp(v,t)}{dt} = \nu\Big[p(v' - h', v'_1, ..., v'_{n-1}) - p(v', v'_1, ..., v'_{n-1})\Big]. \tag{5.34}$$

Now, instead of solving the original partial integro-differential equation we only need to solve the new system of ordinary differential equations. Through this transform we have eliminated the drift term, meaning that the system no longer depends on the density profile gradient, leaving us with a system describing mass transport from one position to another. Now, as the distance between the positions is made practically negligible, the synaptic efficacy under examination will be able to vary in size to even arbitrarily large values.

The right-hand side of the above expression can be replaced by a more general form, because the way the system moves with the original dynamics of the neural system allows the mass transport to be fully determined by the stochastic process. The left side, on the other hand, allows us to use the method of characteristics.

The change of coordinates we performed defines a map from the point s on the line l to a point (x, y) in the state space which gives us two facts to consider. Firstly, a region of the state space is defined by the time evolution of the line segment l, and secondly, the mapping $M : (s, t) \to (x, y)$ must be time-dependent. When simulating the system the relevant state space can be a combination of regions defined by different line segments. As a result of this one has to perform two interleaved steps in order to solve the system. The first step has to account for the deterministic movement of the neurons after which Equation (5.34) will be solved numerically.

5.2.2 Solving the system

Let us look at the conductance based Izhikevich model given by

$$\tau \frac{dV(t)}{dt} = g_l(V(t) - E_L) - g_e(t)(V(t) - E_e) \tag{5.35}$$

$$\tau_e \frac{dg_e(t)}{dt} = -g_e(t) + I_{syn}(t), \tag{5.36}$$

where $V(t), E_L, E_e, \tau, \tau_e, g_l, g_e(t)$ are the membrane potential, the inhibitory and excitatory equilibrium potentials, the membrane time constant, the excitatory membrane time constant, the conductance, and the normalised inhibitory and excitatory conductances, respectively. The parameter $I_{syn}(t)$ describes how the incoming spikes from other neurons affect the neuron in question. This model is conventionally represented by a vector field.

A two dimensional vector v in our vector field now represents a point in the phase space of our system, giving its state in terms of the membrane potential $x(t)$ and some other parameter $y(t)$ such as adaptation or conductance. If we choose two adjacent points from the state space we can construct a strip by integrating the vector field over a time period $z\Delta t$, where $z \in \mathbb{Z}$. These strips make up a geometric grid, an example of which can be seen in Figure 5.2, that defines our system of neurons. A strip $\mathcal{S}$ is now given by

$$\mathcal{S} = \{v_0(t = 0), \ldots, v_0(t = z\Delta t); v_1(t = 0), \ldots, v_1(t = z\Delta t)\},$$

within which a quadrilateral set of points, each set representing a single cell, is defined by

$$\mathcal{C}_i = \{v_0(t = i\Delta t), v_0(t = (i + 1)\Delta t), v_1(t = (i + 1)\Delta t), v_1(t = i\Delta t))\}.$$

It is not necessary for the quadrilateral to be convex as long as it is simple. A convex set is defined as a set C in which for any line segment ab, $\forall c \in ab, c \in C$. To be considered the sets must have enough points in them and the boundaries in the state space are approached through quadrilaterals, the areas of which tend to zero. For simplicity the strips can be numbered based on the order in which they are generated. Here we will use $i \in \{0 \ldots N\}$ to denote unique

strips, where N is the total number of strips. We reserve $i = 0$ for stationary points and there can be 0 or more cells within strip 0. We will denote the number of cells in a strip i by $n(i)$. Each neuron will be seen as a bin the coordinates of which will be given by (i, j), where $j \in \{0, \ldots, n(i)\}$. The neurons will be numbered based on their dynamics as they move in time. This means that neurons given the number j at time t in strip i have moved to number $j+1 \mod n(i)$ at time $t+\Delta t$. This type of movement does not occur in the neurons in strip $i = 0$, as they are considered to be stationary. We will next look at how to interpret the behaviour of these stationary cells.

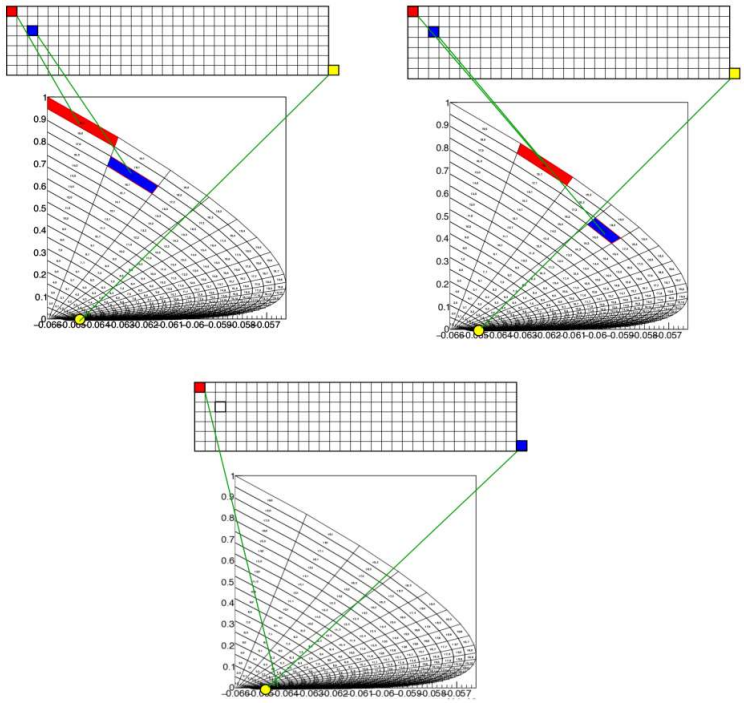

Figure 5.2: An example of a grid produced by the method. Image from [27].

We can use an array $\mathcal{M}$ to represent the density profile of our model. Each element of this array will be associated with the grid in an accumulative manner, so that when we set $c(0) \equiv 0$ and $\forall i \in \{1, \ldots, N\}$

$$c(i) \equiv \sum_{i=1}^{N} n(i-1),$$

then $c(i)$ will give us the amount of cells in all strips up to strip i and $n(i)$ is again the number of cells in strip i. Now we can define a time-dependent index function $\mathcal{I}$ to describe the forward motion of the probability mass in the following manner

$$\begin{cases} i = 0 & \mathcal{I}(i, j, k) = j \\ i \geq 0 & \mathcal{I}(i, j, k) = c(i-j) + (j-k) \mod n(j). \end{cases}$$

However, when the probability mass reaches the end of the strip we are faced with the problem of the same mass reappearing at the start of the strip at the next time step. This can be combatted by removing the probability mass at the start of each strip and assigning a new bin for the removed mass. This is called *reversal mapping* and consists of pairs of coordinates, indicating where the probability mass will be removed from and which bin it will be moved to.

Next we need to account for the synaptic inputs and the specific behaviour of the system at threshold. When considering the synaptic input between individual neurons the received spike trains are assumed to be Poisson processes with known distributions. The synaptic efficacies h can be added together in the case of a continuous distribution. Now the connections between populations can be represented by a tuple (N_c, h, τ_d) where N_c denotes the number of connections from presynaptic neurons onto a single neuron in the population, and τ_d denotes the transmission delay. On the mesoscopic level this leads to a master equation

$$\int_{\mathcal{V}} \frac{dp(v,t)}{dt} dv = \nu \Big\{ \int_{\mathcal{V}_h} p(v',t) dv' - \int_{\mathcal{V}} p(v) \Big\}, \tag{5.37}$$

where $\mathcal{V}$ is an area of the state space, $\mathcal{V}_h$ the same area but translated by the amount of the synaptic efficacy h in the direction of the synaptic conductance, and ν is again the firing rate. This equation describes the probability mass transfer from one bin to another and now determines the right-hand side of the Equation (5.31) allowing us to solve it numerically. The left-hand-side is purely determined by the neuron model we are using, and will give us the grid of strips. We will now assume the density within a single area of the state space to be constant and $\mathcal{V}$ coincides with the bins in the grid. We can then approximate Equation (5.37) by

$$\frac{d\mathcal{M}(i,j,k,t)}{dt} = \nu \left\{ \sum_{(p,q) \in C_h(i,j)} \alpha_{p,q} \mathcal{M}(p,q,k,t) - \mathcal{M}(i,j,k,t) \right\}. \tag{5.38}$$

Translating the bins (i, j) by the synaptic efficacy h will cause overlap. All the bins partially covered by the translated bin can be seen to define a so-called *displacement set*. This set can be found using the Monte Carlo strategy. Performing this linear search procedure repeatedly allows us to locate all of the translated points and that make up the displacement set.

For each coordinate $(p, q) \in C_h(i, j)$ a count $n_{(p,q)}$ is kept making it possible for us to approximate the overlapping area

$$\alpha_{p,q} = \frac{n_{(p,q)}}{N_p}. \tag{5.39}$$

The displacement set now determines a transition matrix $\mathcal{T}$ such that

$$\frac{d\mathcal{M}(t)}{dt} = \mathcal{T} \cdot \mathcal{M}(t), \tag{5.40}$$

which follows from Equation (5.38). Because using this method has allowed us to find the constants $\alpha_{p,q}$ for each bin (p, q) we can solve Equation (5.38) numerically. Now handling the synaptic current consists of three steps; first one updates the index function $\mathcal{I}$ that determines the movement of the probability mass through the grid during the time Δt, second one must implement the reversal mapping as described above, and third one has to solve Equation (5.38) at time Δt.

Because many neuron models have a threshold condition, we need to be able to deal with the sudden jump of the probability mass from one bin to another. The conductance based model defined by Equations (5.35) and (5.36) has a threshold of -55 mV, that corresponds to a vertical boundary in the (V, g) plane. Here the neurons reaching the threshold from below will be removed from the system for the duration of the refractory period, τ_r, after which they will be reintroduced at the point $(V_r, g(t + \tau_r))$, where $g(t)$ is the conductance of the neuron when it hit the threshold. In this model we assume that the conductance variable evolves according to Equation (5.36) and that the spike itself has no effect on it. In some models the effect will be taken into account which usually involves translating each spiking cell in the direction of the second variable. We modulate the threshold activity by constructing a *reset mapping* that maps what are called threshold cells to their corresponding reset cells. The threshold and the reset cells make up a set of all cells that contain the threshold boundary and the reset potential, respectively. The grid being irregular can lead to the master equation transition moving cells into bins above the threshold potential. This can be corrected for when generating the transition matrix. If a generated event ends up moving a point above the threshold value we can look for the closest threshold cell and attribute the event to that instead. The reset phase should be performed immediately after solving the master equation and before the index function is again updated.

The greatest limitation of these types of models is the fact that the finite nature of the Monte Carlo technique leads to some events being lost. This problem can occur both at the edges of the state space as well as close to the stationary points. This leads to gaps in the state space that need to be dealt with adding a new quadrilateral that is made to overlap the gaps. This of course makes the simulation of the system more complicated.

5.3 McKean-Vlasov type dendrite model

The two models we have covered thus far have one thing in common which is the near instantaneous nature of the signal transmission from one neuron to all other points in the network. This assumption fails to take into account that in reality the signal travels along the dendrites of the neuron to reach other neurons in the network, and it takes time for the message to travel across from one point to another. This is one of the major motivations for adding a dendritic component to the model allowing us to take the effect of length and diameter of

the connecting dendrites into account. We do this by tying together the original noisy LIF neuron model and the cable equation (3.21) presented in Chapter 3.3. The model can be found in [28]. As a result of introducing the cable equation, the dynamics at the cell soma are smoothed which makes it impossible for the model to blow up, i.e. one neuron initiates an instantaneous response in all the neurons connected to it producing a spiking cascade large enough to lose all biological relevance. The use of the cable equation allows us to make two helpful generalisations; firstly we can allow for synaptic weights that are not constant, meaning that different neurons are allowed to have differing synaptic strengths between them, and secondly the diffusion coefficient will not need to be constant allowing for a number of different time-dependent coefficients to be used. The variability in the strength of connection between individual neurons is due to the differing dendrite lengths and diameters of the interconnected cells.

In the following section we will derive the mean-field model for a network of neurons with dendritic compartments. We do this in a stepwise manner where we first construct the cell soma by defining its specific dynamics. Then we use the cable equation to derive a representation of the dendrite compartment that will be attached to each soma. The third step is to combine these two by introducing a coupled system in which the equations for both the cell soma and the dendrite hold simultaneously. After the derivation of this system we show the reader how such a system can be solved.

5.3.1 Deriving the system

To start building the mean-field model for a network of neurons that also takes into account the time it takes for an action potential to travel along a dendrite of a neuron, we need to start by creating a model for single neurons in the network which we then take to the mean-field limit in Section 5.3.2. In building the network representation we need to derive models for the soma and the dendrite individually and then combine them together by establishing a coupled system.

We will start building the model by creating a representation of the soma. As stated previously, the underlying dynamics will be given by the noisy LIF neuron which describes the continuous evolution of the electrical potential in the cell soma. When the potential reaches a certain threshold θ the neuron fires an action potential and then resets back to the reset value U_r. Let us denote the potential across the soma of the ith cell at time t by $U_i(t)$ that then evolves according to the following equation

$$U_i(t) = U_i(0) + \int_0^t b(U_i(s))ds + I_i(t) - M_i(t) + \int_0^t \omega(U_i(s))dW_i(s), \tag{5.41}$$

where $t \geq 0$, the potential at time $t = 0$, $U_i(0)$ is assumed to be below the threshold potential, $I_i(t)$ is the input current to the soma of the ith cell at time

t, and $W_i(t)$ is an independent one-dimensional Brownian motion. Here the functions b and ω are defined as differentiable functions such that $b \in \mathcal{C}^1(\mathbb{R})$ and $\omega \in \mathcal{C}^2(\mathbb{R})$. $M_i(t)$ describes the resetting process of the membrane potential after it hits the threshold.

$$M_i(t) = \sum_{k=1}^{\infty} \mathbf{1}_{[0,t]}(\tau_k^i), \tag{5.42}$$

where τ_k^i is the time of the kth spike of the ith neuron. $M_i(t)$ counts the number of spikes before a given time t and so if $0 \leq \tau_k^i \leq t : \mathbf{1}_{0,t}(\tau_k^i) = 1$. The spike times τ are given by

$$\tau_k^i = \inf\{t \geq \tau_{k-1}^i : U_i(t-1) \geq \theta\}, \tag{5.43}$$

where $t > 0$ and whenever $U_i(t-1)$ reaches the threshold θ then $U_i(t)$ has to be the reset potential U_r, as a spike is always followed by a reset in the membrane potential. $M_i(t)$ is an integer-valued function that has a voltage-dependent update process, meaning that every time U_i reaches threshold and thus causes a spike, $M_i(t)$ will be updated such that when U_i reaches θ

$$M_i(t) = M_i(t-1) + 1.$$

Next we will need to look at the cable equation that will give us a good description for the dendrite of our cell. We take a cable $\mathcal{R}$ that is uniform, one-dimensional, and infinite, and attach the soma to it, so that it will be located at position 0 along the cable. Let $V_i(t,x)$ be the membrane potential at a given position $x \in \mathcal{R}$ along the dendritic tree of the neuron i at the time t. The evolution of the membrane potential along the dendrite is then given by the cable equation

$$\frac{\partial V_i(t,x)}{\partial t} = \frac{1}{2}\frac{\partial^2 V_i(t,x)}{\partial x} - \gamma V_i(t,x) + f_e^i(t,x), \tag{5.44}$$

where $f_e^i(t,x)$ is the applied current density at the position $x \in \mathcal{R}$ at a given time $t \geq 0$, for some $\gamma > 0$. In Figure 3.1 a piece dendrite is described in terms of the cable equation.

In order to describe the network behaviour of the cell population with dendritic compartments we need to couple Equations (5.41) and (5.44) together. The applied current density $f_e^i(t,x)$ in Equation (5.44) has to depend on all of the presynaptic spike trains reaching neuron i, whereas the input current $I_i(t)$ in Equation (5.41) has to depend on the potential across the dendritic tree of the ith neuron. The relationship between the input current and the potential is proportional

$$I_i(t) \propto V_i(t,0), \tag{5.45}$$

for all times $t \geq 0$, where the $V_i(t,0)$ is the potential at position 0 of the cable where the soma is located. For the applied current density we will use the following representation

$$f_e^i(t,x) = \frac{1}{S_i^N} \sum_{j=1}^{N} J_{ij} \rho(x) \sum_{k=1}^{\infty} \delta_0(t - \tau_k^j), \tag{5.46}$$

where $\sum_k \delta_0(t - \tau_k^i)$ is the spike train of the neuron j, δ_0 is the Dirac delta distribution at 0, $\rho : \mathbb{R} \to \mathbb{R}$ is a smooth and bounded function describing the density of the synapses of the dendritic tree connecting neuron i to neuron j, $J_{ij} \geq 0$ is the strength of the connections between neurons i and j such that $i, j \in \{1, \ldots, N\}$. Here we have made the simplifying assumption that the synapses are distributed homogeneously along the whole dendritic tree. Above $S_i^N = \sum_{j=1}^{N} J_{ij}$, meaning that we multiply the synaptic density of each point x by the proportional synaptic strength of the connected neurons. This allows us to suppose that although the synaptic distribution is homogeneous, the amount of synaptic current relayed from neuron to neuron depends on the strength of the connecting synapses. It is important to point out that this does not mean that the connection strength would be homogeneous, instead they are given by J_{ij}. If we now combine Equations (5.41), (5.44), (5.45), and (5.46) we can establish a coupled system

$$\begin{cases} \dfrac{\partial V_i(t,x)}{\partial t} = \dfrac{1}{2} \dfrac{\partial^2 V_i(t,x)}{\partial x} - \gamma V_i(t,x) \\ + \dfrac{\rho(x)}{S_i^N} \displaystyle\sum_{j=1}^{N} J_{ij} \sum_{k=1}^{\infty} \delta_0(t - \tau_k^j), \\ U_i(t) = U_i(0) + \displaystyle\int_0^t b(U_i(s))ds + V_i(t,0) - M_i(t) \\ + \displaystyle\int_0^t \omega(U_i(s))dW_i(s) \end{cases} \tag{5.47}$$

for $t \geq 0$ and $i \in \{1, \ldots, N\}$. In the next section we take this coupled system to the mean-field limit thus deriving a model in which the behaviour of each neuron in the theoretically infinite population tends to an average of the population behaviour.

5.3.2 Solving the system

Using this coupled system we can derive a self-contained system representation for the membrane potentials $U_i(t), i \in \{1, \ldots, N\}$, such that the behaviour of each neuron can be accounted for, as it is determined by the potential across the soma. The first Equation in (5.47) can be solved using a *Green's function*, as in Definition 3.4, given by

$$\mathcal{G}(t,x) = \frac{1}{\sqrt{2\pi t}} e^{-\gamma t} e^{\frac{-x^2}{2t}}, \tag{5.48}$$

where $t > 0$ and $x \in \mathcal{R}$. This is the fundamental solution to the cable equation, and $\forall i \in \{1, \ldots, N\}, t > 0$, and $x' \in \mathcal{R}$

$$\begin{aligned} V_i(t,x') &= [\mathcal{G}(t,\cdot) * V_i(0)](0) \\ &\quad + \int_0^t \int_{-\infty}^{\infty} \frac{\mathcal{G}(t-s, x-x')}{S_i^N} \rho(x) \sum_{j=1}^{N} J_{ij} \sum_{k=1}^{\infty} \delta_0(s - \tau_k^j) dx ds, \end{aligned}$$

where $*$ denotes convolution and $\sum_k \delta_0(s-\tau_k^j) = \frac{d}{ds} M_j(k)\, \forall s \geq 0, j \in \{1, \ldots, N\}$. This is due to the fact that the spike train $\sum_k \delta_0(s - \tau_k^j)$ has the same distribution as the derivative of the spike count before time t, as whenever there is a spike in the spike train we add one, as well as when the spike count is updated we add one, giving us a derivative of zero between spikes and a derivative of one when a spike occurs. When we evaluate $V_i(t,x')$ at $x' = 0$, this yields

$$\begin{aligned} V_i(t,0) &= [\mathcal{G}(t,\cdot) * V_i(0)](0) \\ &\quad + \int_0^t [\mathcal{G}(t-s,\cdot) * \rho](0) \frac{d}{ds} \left(\frac{1}{S_i^N} \sum_{j=1}^{N} J_{ij} M_j(s) \right) ds. \end{aligned} \tag{5.49}$$

We assume that there are no synapses on the soma which is not an uncommon assumption to make, as this is frequently done in biological literature. This means that for the function describing the synapse density of the dendritic tree $\rho : \mathbb{R} \to \mathbb{R}$ the density at position 0, the soma, is zero. So we have $\rho(0) = \rho''(0) = 0$. This means that there is no presynaptic transmission that would reach the soma instantaneously, and that the input current to the soma of the ith cell $V_i(t,0)$ is continuous. Using this assumption and integrating Equation (5.49) by parts

$$\begin{aligned} V_i(t,0) &= [\mathcal{G}(t-s,\cdot) * Vi(0)](0) \\ &\quad + \int_0^t [\mathcal{G}(t-s,\cdot) * \rho](0) \frac{d}{ds} \left(\frac{1}{S_i^N} \sum_{j=1}^{N} J_{ij} M_j(s) \right) ds \\ &= [\mathcal{G}(t-s,\cdot) * Vi(0)](0) \\ &\quad + \frac{1}{S_i^N} \sum_{j=1}^{N} J_{ij} \int_0^t [\mathcal{G}(t-s,\cdot) * \rho](0) \frac{d}{ds} M_j(s) ds \\ &= [\mathcal{G}(t-s,\cdot) * Vi(0)](0) \\ &\quad + \frac{1}{S_i^N} \sum_{j=1}^{N} J_{ij} \Bigg([\mathcal{G}(t-s,\cdot) * \rho](0) M_j(s) \\ &\quad + \int_0^t \frac{d}{ds} [\mathcal{G}(t-s,\cdot) * \rho](0) M_j(s) ds \Bigg), \end{aligned}$$

where

$$\begin{aligned}[\mathcal{G}(t-s,\cdot)*\rho](0) &= \int_{-\infty}^{\infty} \mathcal{G}(t-s,0-\Delta)\cdot\rho(0)d\Delta \\ &= \int_{-\infty}^{\infty} \mathcal{G}(t-s,0-\Delta)\cdot 0 d\Delta \\ &= 0,\end{aligned}$$

leaving us with

$$\begin{aligned}V_i(t,0) &= [\mathcal{G}(t,\cdot)*V_i(0)](0) \\ &\quad + \sum_{j=1}^{N}\frac{J_{ij}}{S_i^N}\int_0^t \frac{d}{ds}[\mathcal{G}(t-s,\cdot)*\rho](0)M_j(s)ds.\end{aligned} \tag{5.50}$$

When we plug this into the second Equation in (5.47) we arrive at the self-contained system

$$\begin{aligned}U_i(t) &= U_i(0) + K_{V_i(0)}(t) + \int_0^t b(U_i(s))ds \\ &\quad + \sum_{j=1}^{N}\frac{J_{ij}}{S_i^N}\int_0^t G_\rho(t-s)M_i(s)ds - M_i(t) + \int_0^t \omega(U_i(s))dW_i(s),\end{aligned} \tag{5.51}$$

where $G_\rho(t-s) = \frac{d}{ds}[\mathcal{G}(t-s,\cdot)*\rho](0)$ and $K_{V_i(0)}(t) = [\mathcal{G}(t,\cdot)*V_i(0)](0)$. Here G_ρ and $K_{V_i(0)}$ are twice continuously differentiable as well as bounded with bounded derivatives and $G_\rho(0) = G_\rho'(0) = 0$.
Now we have the following system

$$\begin{cases} U_i(t) = U_i(0) + K(t) + \int_0^t b(U_i(s))ds \\ + \sum_{j=1}^N \frac{J_{ij}}{S_i^N}\int_0^t G_\rho(t-s)M_j(s)ds - M_i(t) + \int_0^t \omega(U_i(s))dW_s^i, \\ S_i^N = \sum_{j=1}^N J_{ij}, \\ M_i(t) = \sum_{k=1}^\infty 1_{[0,t]}(\tau_k^i), \\ \tau_k^i = \inf\{t \geq \tau_{k-1}^i : U_i(t) \geq 1\}, \end{cases} \tag{5.52}$$

for $t \geq 0$ and $i \in \{1,\dots,N\}$, where $k \in \mathbb{N}\setminus\{0\}$, and $\tau_0^i = 0$. Note that between the spiking times the potentials U_i will evolve independently of each other and simply follow the stochastic differential equation. When the system does spike, that is when one of the potentials U_i reaches the threshold θ from below, we will set $M_i(t) = M_i(t) + 1$, where $M_i(t)$ on the right-hand side approaches 1 from below. This updates the SDEs. When we finally take the number of neurons N to infinity the system (5.52) transforms into the mean-field equation

$$\begin{cases} U(t) = U(0) + K(t) + \int_0^t b(U(s))ds \\ + \int_0^t G_\rho(t-s)\mathbb{E}(M(s))ds - M(t) + \int_0^t \omega(U(s))dW(s), \\ M_t = \sum_{k=1}^\infty 1_{[0,t]}(\tau_k), \\ \tau_k = \inf\{t \geq \tau_{k-1} : U(t) \geq \theta\}, \end{cases} \tag{5.53}$$

for $k \in \mathbb{N} \setminus \{0\}$, $\tau_0 = 0$, and $U(t)$ approaches θ from below. When the population grows large enough we can assume that the sum of the averaged synaptic weights $\sum_{j=1}^{N} \frac{J_{ij}}{S_i^N}$ is one and the sum of the spike count of individual neurons $M_j(s)$ converges to the expectation of the population spike count $\mathbb{E}(M(s))$. This is now a mean-field equation of McKean-Vlasov type, as the right side of the equation is dependent on the distribution of the solution. The following assumptions are made for the coefficients K, b, σ, and G_ρ, and the initial condition $U(0)$

- $K : [0, \infty) \to \mathbb{R}$ is bounded and twice differentiable with bounded derivatives,
- $b \in \mathcal{C}^1(\mathbb{R})$ with bounded derivatives, and set $\Lambda_b = \max\{\|b'\|_\infty, b(0)\}$, such that
$$|b'(x)| \leq \Lambda_b, \quad |b(x)| \leq \Lambda_b(1 + |x|), \quad x \in \mathbb{R},$$
- $\omega \in \mathcal{C}_b^2(\mathbb{R})$ and there exists a constant $\Lambda_\sigma > 0$ such that
$$\Lambda_\sigma^{-1} \leq \sigma(x) \leq \Lambda_\sigma, \quad |\sigma'(x)|, |\sigma''(x)| \leq \Lambda_\sigma, \quad x \in \mathbb{R},$$
- $G_\rho : [0, \infty) \to \mathbb{R}$ is bounded and twice differentiable, with bounded derivatives, such that
$$G_\rho(0) = G_\rho'(0) = 0,$$
- $U(0) \in (-R, \theta)$ almost surely for some $R \geq \theta$ and is such that

$$\sup_{t \in (0,T]} \int_{-\infty}^{\theta} (\theta - x) t^{-\frac{3}{2}} e^{-\frac{(\theta - x)^2}{\Lambda_\sigma t}} \mathbb{P}(U(0) \in dx) < \infty \quad \forall T > 0. \tag{5.54}$$

Because the system (5.53) is discontinuous, we formulate it into a continuous expression, for convenience. This is achieved by adding the terms $U(t)$ and $M(t)$ together to bring about a new variable, $Z(t)$ such that

$$Z(t) := U(t) + M(t).$$

Now the Equation (5.53) takes on the following form

$$\begin{cases} Z(t) = U(0) + K(t) + \int_0^t b(Z(s) - M(s))ds \\ + \int_0^t G(t-s)\mathbb{E}(M(s))ds + \int_0^t \sigma(Z(s) - M(s))dW(s), \\ M(t) = \lfloor (\sup_{s \leq t} Z(s))_+ \rfloor, \\ \tau_k = \inf\{t \geq 0 : Z(0) \geq k\}, k \in \mathbb{N} \setminus \{0\}, \tau_0 = 0. \end{cases} \tag{5.55}$$

The two main results in the Inglis et al. paper [28], are that the solution to system (5.53) exists and is unique. This means that the system can truly be

used to evaluate the dendritic compartment model as it is solvable and the acquired solution is one of a kind in the sense that there is no other solution that would satisfy the equations in the system. They also show that, given some conditions about the synaptic weights J_{ij}, the solution converges to the limit equation. Using the continuous expression in Equation (5.55) a single cell system can be derived

$$
\begin{cases}
Z_i(t) = U_i(0) + K(t) + \int_0^t b(Z_i(s) - M_i(s))ds \\
+ \sum_{j=1}^{N} \frac{J_{ij}}{S_i^N} \int_0^t G(t-s)(M_j(s))ds + \int_0^t \sigma(Z_i(s) - M_i(s))dW_i(s), \\
M_i(t) = \lfloor (\sup_{s\in[0,t]} Z_i(s))_+ \rfloor, \\
\tau_k^i = \inf\{t \geq 0 : Z_i(0) \geq k\}, k \in \mathbb{N} \setminus \{0\}, \tau_0^i = 0.
\end{cases} \tag{5.56}
$$

by replacing the averaged expressions again with the original descriptions of each neuron i. As the family of laws governing the synaptic weights J_{ij} in the single cell system is tight, the convergence can be proved using the property that the laws under all of the limit points of system (5.56) must be the same as the law of the unique solution of the limit equation. The formal proof of this is out of the scope of this thesis and can be found in its entirety in [28].

6 Conclusions

The three mean-field models discussed in this thesis were chosen based on their different properties. First we looked at the ensemble density model that uses the Fokker-Planck formalism to derive a tractable partial differential equation which converges to the same stable attractors as the underlying intractable system of LIF neurons. As this method requires us to use the diffusion approximation we are limited to the Ornstein-Uhlenbeck process as well as neuronal networks with asynchronous activity. If the original system has multiple steady states it is likely that the Fokker-Planck equation is not an accurate global approximation to the chemical master equation. [18]

The problems arising from the diffusion approximation can be avoided with the change of coordinates performed in the Marc de Kamps model in Section 5.2. As previously stated, where the Fokker-Planck approach relies on the diffusion approximation, the computational geometry method allows for different stochastic processes to be considered. However, when pushed to reproduce results at the diffusion limit the Fokker-Planck equation is found to be more efficient. Nevertheless, this method can accurately model delta synapses and is better at dealing with density profile discontinuities as well as depicting populations with synchrony which always fails when using the Fokker-Planck equation. In this case the PDE arising from the Chapman-Kolmogorov equation can be transformed into an ODE in the form of a Poisson master equation making it easier to solve analytically. This transform eliminated the drift term completely, removing the dependence of the system on the density profile gradient. As this method is also applicable to both 1D and 2D models, it offers a larger repertoire of applications compared to most other models. Still, the downside of the method proposed by de Kamps et al. [27] is the computational burden, as without performing the diffusion approximation the system retains its complexity throughout the mathematical analysis.

One problem that the first two models face is the gross approximation of instantaneous propagation of the action potential. The third model we looked at added a dendritic compartment to the single neuron model by introducing the cable equation into the system. This allows for differing synaptic weights as well as general diffusion constants due to the smoothing kernel G. It describes the lack of synapses in the soma of the cell and the smooth transition of the signal to the post-synaptic cell. The model assumes homogeneously distributed synapses along the dendrites which – though biologically accurate in some cases – is clearly not always the case. An inhomogeneous distribution of synapses along the dendritic tree would require a different approach. The model introduced by Inglis et al. [28] also lacks noise in terms of spike transmission along the dendrites. Adding this to the model would make it more accurate but again more burdensome with respect to computation.

References

[1] ALLEN INSTITUTE. *Allen Institute open for science*. Online. Updated 2019. Viewed 12.12.2019. http://www.allenintitute.org/.

[2] Peter Dayan, L. F. Abbott. *Theoretical Neuroscience*. Massachusetts: MIT Press, 2001.

[3] K. M. Dabrowski, D. J. Castaño, J. L. Tartar. *Basic neuron model electrical equivalent circuit: an undergraduate laboratory exercise*. Journal of Undergraduate Neuroscience Education 7 (2013) 12(1) 49-52.

[4] Pasquale De Michele. *Analysis, tuning and implementation of neuronal models simulating Hippocampus dynamics*. Doctoral thesis, 2015.

[5] Dimitris Pinotsis, Peter Robinson, Peter beim Graben, Karl Friston. *Neural masses and fields: modeling the dynamics of brain activity*, Frontiers Computational Neuroscience 8 (2014) 149.

[6] Alan Hodgkin, Andrew Huxley. *A quantitative description of membrane current and its application to conduction and excitation in nerve*. Journal of Physiology 117(4) (1952) 500–544.

[7] Tiina Manninen, Marja-Leena Linne, Keijo Ruohonen. *Developing Itô stochastic differential equation models for neuronal signal transduction pathways*. Computational Biology and Chemistry 30(4) 280-291, 2006.

[8] Wulfram Gerstner, Werner M. Kistler, Richard Naud, Liam Paninski. *Neuronal Dynamics* Online book. Updated 2014. Viewed 9.12.2019. https://neuronaldynamics.epfl.ch/online/.

[9] Eugene M. Izhikevich. *Simple Model of Spiking Neurons*, IEEE Transactions on Neural Networks 14(6) (2003) 1569-1572.

[10] Erik De Schutter. *Computational modeling methods for neuroscientists*, MIT Press, 2010.

[11] David Sterrat, Bruce Graham, Andrew Gillies, David Willshaw. *Principles of Computational Modelling in Neuroscience*. Cambridge University Press, 2011.

[12] Stefanescu RA, Jirsa VK (2008) *A Low Dimensional Description of Globally Coupled Heterogeneous Neural Networks of Excitatory and Inhibitory Neurons*. PLoS Comput Biol 4(11): e1000219. https://doi.org/10.1371/journal.pcbi.1000219.

[13] Gustavo Deco, Viktor Jirsa, Peter Robinson, Michael Breakspear, Karl Friston. *The Dynamic Brain: From Spiking Neurons to Neural Masses and Cortical Fields*. PLOS Computational Biology 4(8) (2008), e1000092. https://doi.org/10.1371/journal.pcbi.1000092.

[14] Prasanna Sahoo. *Probability and mathematical statistics*. Department of Mathematics University of Louisville. 2008.

[15] Jean-François Le Gall. *Brownian Motion, Martingales, and Stochastic Calculus*. Springer International Publishing, 2016.

[16] Lawrence C. Evans. *Partial Differential Equations, 2nd edition*. Graduate Studies in Mathematics vol 19, 2015.

[17] Arthur L. Schoenstadt. *An Introduction to Fourier Analysis*. Department of Applied Mathematics, Naval Postgraduate School. 2005.

[18] Werner Dubitzky, Olaf Wolkenhauer, Kwang-Hyun Cho, Hiroki Yokota. *Encyclopedia of Systems Biology*. Springer, 2013.

[19] Kenneth Schweizer. *Brownian motion*. Lecture notes, 2019.

[20] J. L. Garcia-Palacios. *Introduction to the theory of stochastic processes and Brownian motion problems*. Lecture notes, 2004.

[21] Raúl Toral. *Stochastic Processes*. Lecture notes, 2014.

[22] Jim Frost. *Statistics by Jim*. Online. Updated 2019. Viewed 25.07.2019. https://statisticsbyjim.com/basics/central-limit-theorem/.

[23] Peter W. Glynn. *Diffusion Approximations*. Book chapter. Elsevier, 1990.

[24] Mikko Lehtimäki, Ippa Seppälä, Lassi Paunonen, Marja-Leena Linne. *Accelerated simulation of a neuronal population via mathematical order reduction*. Proceedings of the IEEE International Conference on Artificial Intelligence Circuits and Systems, 2020.

[25] Karl Sigman. *Discrete time Markov Chains*. Lecture notes, 2009.

[26] Diego Fasoli. *Attacking the brain with neuroscience: mean-field theory, finite size effects and encoding capability of stochastic neural networks*. Doctoral thesis. Université de Nice-Sophia Antipolis, 2013.

[27] Marc de Kamps, Mikkel Lepperod, yi Ming Lai. *Computational Geometry for Modeling Populations: from Visualization to Simulation*, PLOS Computational Biology 15(3) (2019), e1006729. https://doi.org/10.1371/journal.pcbi.1006729.

[28] J. Inglis, D. Talay. *Mean-Field Limit of a Stochastic Particle System Smoothly Interacting through Threshold Hitting-Times and Applications to Neural Networks with Dendritic Component*. SIAM Journal of Applied Dynamical Systems 15(1) (2016) 195-234.